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Archives of Dermatology and Syphilology

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THE EVER CHANGING THERAPY OF SYPHILIS*

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When the epidemic of syphilis reached the continent late in the fifteenth century, physicians were loath to treat patients who had the disease, because they knew nothing about it. Up to this time and for centuries later, the practice of medicine was more or less a matter of empiricism. Consequently, the sufferers fell into the hands of charlatans, until from shame the ethical practitioners were forced to treat persons with this malady.

DRUGS USED AND METHODS OF THEIR ADMINISTRATION

Mercury.—In 1497, Jean di Vigo, supported by others, recommended the use of mercury, and from this time on the therapy of syphilis has had a never ending motif.

Physicians advocating the use of mercury were deeply impressed by the success of their remedy, while their opponents were as deeply impressed by its failure. Such a period of therapeutic hysteria then supervened that the use of mercury was practically discarded for almost three hundred years, with only such periodic revivals as served to throw it again into disrepute.

It is now realized that if mercury had been properly used during this long period, the world would not, in all probability, have been "syphilized" while it was being civilized.

Guaiacum.—During this intervening space of time, the therapeutists in their blind search for some agent to combat this disease, used the entire list of the then known substances. For a while, guaiacum held the center of the stage, and the supporters of the use of this drug were as enthusiastic in its praises as are those who today advocate the malaria treatment for syphilis.

Sudorific Wood.—The distillation and concoction of sudorific woods were used in profusion, and it is conceivable that any beneficial action

*Read at the Fiftieth Annual Meeting of the American Dermatological Association, May, 1927.

they had might have been due to the small amount of residual salts which were a part of their composition.

At this time the bark of the cinchona tree was introduced from South America, and a great number of patients with malarial syphilis were benefited by the relief from malaria. The greatest of all wood infusions then took its place among the remedies, and the use of sarsaparilla tea was introduced; even in modern times this holds first place as a spring tonic by most rural natives. Citrous fruits were also used in abundance in the treatment of patients with syphilis.

Opium.—Late in the seventeenth century opium was introduced, but was soon forgotten. A century later, however, during the Revolutionary War, its use was revived by two English surgeons. They produced such a perfect dream state by its use that both the patient and the physician soon forgot the disease. From this blissful semianesthetic state they were rudely awakened by the administration of nitric acid and oxidized metals, which seemed to produce a little benefit.

Iodine.—The second great epoch in the treatment of patients with this disease was in the early part of the nineteenth century. Iodine, introduced by Martini and popularized by Lugol, became the most successful of all antisyphilitic remedies. Late manifestations disappeared under its administration, and patients with cases that were otherwise intractable became marvelously cured. The therapeutic advance made by the introduction of this drug has not been surpassed, and this remedy today stands out as one of the most efficient. During all this time, mercury and iodine formed the greatest combination that has ever been used in the treatment of patients with syphilis, until the advent of Ehrlich's discovery in 1908.

Consideration should be given to these two remedies and their various combinations. Since the advent of arsphenamine, the administration of mercury and iodine has almost become a lost art. Therapeutists are prone to lay aside an efficient weapon in their eagerness to try a new one and to forget that they achieved better results with the old one.

In the treatment of patients who have late cutaneous manifestations, involvement of the bones and gummatous formations in the liver and brain, the iodides and mercury are best. In this type of syphilis it is far better not to introduce the arsenical compounds, because they are likely to produce the effect one is trying to avoid.

From 1821 to 1910 the treatment of patients with syphilis was placed on a rational basis. This space of time represents a period when all therapeutists were in accordance concerning the efficiency of this form of treatment. Their observations, on the whole, were of more value than are the chaotic methods of the present day, for phy-

sicians were able to observe many of their syphilitic patients through three generations. The fact that many patients were cured proves the efficiency of their methods. Practically all the pathologic manifestations were observed and described, while the clinical acumen of these observers has not been surpassed. It is true that many divergences of certain types of syphilis have been added, but practically no new types have been included. Without laboratory facilities, the present day syphilographer would undoubtedly be surpassed by many of the older diagnosticians. James Nevins Hyde, Abner J. Post, George Henry Fox and others are representatives of this school.

Arsphenamine.—In spite of these keen observations and a fairly standard method of treatment, the results were far from satisfactory. Scientific minds began to search for some organic combination of metals which, given in a massive dose, would cure the patient and finally eliminate the disease from the human race. Arsphenamine, one of the many metallic combinations, devised by Ehrlich, seemed to be the most promising; while he never held it to be an absolute curative agent, almost the entire medical profession accepted it as such. For a short period of time, this preparation no doubt did more harm than good. From both fear and ignorance, patients were undertreated, and it is an axiom that a little treatment is worse than none. Somatic recurrences were so common that the literature was filled with instances of reinfection.

Following the discoveries of Schaudine and Hoffman and Ehrlich, a renewed stimulus appeared, which was responsible for the finest research work ever devised by man in any line of endeavor, with the exception of the classic work of Pasteur.

For a period of ten years the use of the arsenicals overshadowed all other therapeutic measures, and almost caused this remedy to be discarded. Many accusations were made, but few were sustained.

Gaucher was of the opinion that when other parts than the central nervous system were involved, arsenic would produce the various sclerotic changes in the tissues that syphilis produced; at first glance, this would seem to be true, but in view of later experiences, this must be regarded as a rapid cumulation of a process already started by the disease. The first reaction between the tissue and the organism is the swift response of the lymphocytes to the attacked area, and the inevitable result of this lymphocytic infiltration is the formation of connective tissue. If this involvement is in a blood vessel or the liver, the use of an arsphenamine preparation would simply shorten the period of time during which this pathologic change takes place, and would not allow any time for compensatory circulation or increased activity of cells. This would naturally interfere with the functioning of the parts involved; therefore, it is wise never to use arsphenamine for this type of pathologic process. It is advisable to use the slower anti-

syphilitic treatments, which will allow the diseased parts to compensate for their disability.

During this decade, however, there were those who believed that the various combinations of mercury and iodides should be used with the arsenicals, and a therapeutic system has been worked out which is efficient in those cases in which the patients do not show central nervous system manifestations.

It is the belief of some that the apparent increase in cases of syphilis of the central nervous system has been caused by arsphenamine, and the chief supporters of this opinion are the Anglo-Saxons and the Gauls. We shall consider the possible causes if such an increase has occurred. The discovery of *Spirochaeta pallida* by Schaudine and Hoffman, the Bordet-Wassermann reaction, the demonstrations of *Spirochaeta pallida* in the spinal cord of tabetic patients by Noguchi, the recovery of live spirochetes from the brain of patients with general paralysis by Wile, and the almost infallible observations in the cerebrospinal fluid have made possible the greatest accuracy in the diagnosis of any disease. The inevitable results of this procedure have added great numbers of hitherto unsuspected syphilitic patients to this classification. Therefore, any comparison between the modern statistics and the old would be absurd. Gallaleo might as well have denied the discovery of new constallations by modern astronomers because he could not see them with his crude instruments.

When a careful survey is made of all the cases of syphilis of the central nervous system, it will be found in nearly every instance that the patients received insufficient treatment in the beginning of their disease, and that treatment was not resumed until the symptoms involving the central nervous system appeared. Accurate work has not been done up to date to prove that these patients are more intractable to treatment than those who have not received any treatment. Some of this uncertainty can be avoided by examination of the spinal fluid of patients with early syphilis before treatment is instituted, since it is generally agreed that involvement of these tissues in the large majority of cases takes place in the beginning of the disease. Treatment is instituted in an early case in a patient with unsuspected involvement of the central nervous system, and for some reason this procedure is not carried out. The result is control of somatic symptoms, but practically no influence on the activity of the organism in the brain and spinal cord. It may even stimulate the organisms to greater growth or make them resistant to further treatment. Surely, this is not the fault of the arsphenamine itself, but must be attributed to the indifference of the patient or to the ignorance of the physician. We do not believe that arsphenamine properly used has increased the proportion of cases of involvement of the central nervous system.

Intraspinal Treatment.—There still remains the treatment of patients with syphilis of the central nervous system. Realizing the futility of these remedies in tabes and general paralysis, Swift and Ellis devised intraspinal treatment, which immediately divided the therapeutists into two groups: those for and those against this method. Undoubtedly, this method was beneficial for a great number of patients, but unfortunately, many of the proponents of this type of treatment became its opponents, and thus a valuable procedure was thrown into disrepute. Certain physicians claimed that whatever benefit was secured was due to the withdrawal of the spinal fluid, and that valuable time was lost in this procedure.

Tryparsamide.—A new arsenical preparation was devised from the petavalent group, tryparsamide, and first used in the State Asylum of Wisconsin, with astounding results. It was claimed that while this preparation did not directly affect the serology, it had a decidedly beneficial action on patients with general paralysis, and that 50 per cent of them showed considerable remissions in their symptoms. Yet—the ideal remedy had not been found. This marks the end of the use of metallic compounds in the treatment of patients with this type of the disease.

Malaria Plasmodium.—Despairing of results in this line of treatment, and after a long line of experiments with foreign proteids, Wagner von Jauregg, in the Vienna Clinic, came to the conclusion that the malaria plasmodium might be of benefit in treating patients who had syphilis of the central nervous system. His investigations were received with acclaim by most Europeans, but were not accepted by Americans until three years ago.

The use of animal parasites then became popular, and inoculations with the spirillum of relapsing and ratbite fever were advocated. About the same results were claimed for all. Proponents of these three methods of treatment claim approximately 50 per cent remissions in their cases, but they say that when one method fails another might succeed.

It is believed that the judicious combination of arsenic, mercury and the iodides will cure the majority of patients who do not have involvement of the nervous system or cardiovascular disease. Yet a certain percentage of patients remains who, due either to the virulence of the organism or to the nonresponse to these methods, are not cured. This group is represented by those who have either a persistent positive Wassermann reaction or a persistent recurrence of symptoms and signs while under treatment.

Bismuth Salts.—Levedite conceived the idea that some other metal might fill the vacancy in this therapeutic break, and as a result of his

experiments, advocated the use of bismuth salts. It is too early to prognosticate the value of this remedy, but it seems to be securing a definite foothold among the standard remedies. Enough work has been done to show that in many instances it will stop recurrences or change a persistent positive Wassermann reaction. Whether or not these changes are permanent remains to be seen.

COMMENT

The ideal remedy has not nearly been approached, and probably never will be, for the pathologic processes of syphilis prohibit the resolution of connective tissue or the complete restoration of injured cells. Therefore one should not attempt to cure patients of tabes, general paralysis and cardiovascular disease, but to prevent these diseases. The fundamental fact remains that the cure of patients who have syphilis depends on the eradication of the condition during the early stages. Unfortunately, the majority of patients who have general paralysis and tabes are obliged to seek treatment from the general practitioner, who, confronted by the great variety of therapeutic procedure, is lost in the maze of opinions and technicalities. Urged on by his inferiority complex, he begins a certain line of procedure, only to drop it for another; and those who are supposed to be versed in these procedures have not given him any therapeutic basis on which to rely. It is impossible for the specialist to treat every patient who should be treated by him, but he should recommend methods of treatment by which a less fortunate colleague may be guided.

HEPATITIS OF EARLY SYPHILIS

BLOOD BILIRUBIN DETERMINATIONS AS A POSSIBLE AID IN DIAGNOSIS AND AS A GUIDE TO TREATMENT

REPORT OF A CASE *

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Because of its size, activity and vascularity, one would expect the liver to be infected frequently with *Spirochaeta pallita* during the initial stage of spirochetemia. While postmortem statistics (Symmers [1] and McNeil [2]) show that this is true, only a few cases of early involvement are recognized clinically. The clinical cases of syphilitic hepatitis are divided into two groups: first, a mild hepatitis; second, a severe hepatitis or icterus gravis. The incidence of the mild type, according to Wile,[3] is recorded in 0.5 per cent of all cases. Stokes [4] quoted Werner's incidence at 0.37 per cent and Reimer's at 3 per cent, while Stokes has seen only one case of undoubted mild hepatitis in a survey of 300 cases of early syphilis.

The second type of hepatitis, the severe form, is a complication of syphilis that is seen more rarely. Most authors could report only one case, although Richter has recorded three cases. Osler [5] stated that 10 per cent of all cases of acute yellow atrophy occur during early syphilitic disease.

PATHOLOGY

The pathologic changes which occur in cases of mild hepatitis and which produce jaundice were described by Kolmer [6] as an obstruction of the common bile duct due to catarrhal duodenitis; this, in turn, may be due to a syphilitic exanthem of the mucosa, or it may be the result of con-

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* From the Department of Dermatology, Crowell Clinic.

* Read at the Fiftieth Annual Meeting of the American Dermatological Association, May, 1927.

1. Symmers, Douglas: Anatomic Lesions of Late Acquired Syphilis, J. A. M. A. **66**:1457 (May 6) 1916.

2. McNeil, H. L.: Syphilis of the Liver, Am. J. Syph. **1**:738 (Oct.) 1917.

3. Wile, U. J.: Two Unusual Phases of Hepatic Syphilis, Arch. Dermat. & Syph. **1**:656 (June) 1920.

4. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1926, p. 769.

5. Osler, William: Modern Medicine, Philadelphia, Lea and Febiger, 1914, vol. 3, p. 473.

6. Kolmer, J. A.: Chemotherapy, with Special Reference to Treatment of Syphilis, Philadelphia, W. B. Saunders Company, 1926, p. 984.

striction of the bile ducts by the pressure from edema and cellular exudates in the perivascular spaces invaded by *Spirochaeta pallida,* in addition to involvement of cells of the liver at the periphery of the lobules.

SYMPTOMATOLOGY

The symptoms of the mild type are similar to those of an acute catarrhal jaundice. The enlargement of the liver with a sensation of tenderness is a constant sign. Patients with this type of syphilis respond readily to antisyphilitic treatment. If the patients are untreated, however, the condition in some of these cases progresses to an acute yellow atrophy.

The symptoms of icterus gravis syphiliticus, as described by Wile,[7] are those of acute yellow atrophy, differing from other cases only in that the patients respond to antisyphilitic treatment when it is instituted early. The onset is usually insidious with a mild but steadily deepening jaundice. It is accompanied by malaise, vomiting and constipation, but without other marked gastro-intestinal symptoms. Muscular pains and severe abdominal cramps are common. Fever may or may not be present. A toxemia similar to that seen in typhoid fever is often present. Hemorrhagic symptoms have been reported by some authors. The second stage of the disease is characterized by a decided increase in toxemia. The liver, which has often been enlarged to an extreme degree, diminishes rapidly in size, and maniacal symptoms associated with intense headache and disturbances of vision appear. In the later stages, the symptoms frequently resemble those of meningitis, and the patient dies in coma.

DIAGNOSIS

Jaundice is rarely seen in early cases of syphilis. It may be either a mild obstructive type of jaundice, or it may be associated with a true hepatitis. Since the symptoms of both the mild form and nonsyphilitic catarrhal jaundice are similar, they are distinguished with difficulty. The differential criteria are the presence of early syphilis and prompt response to antisyphilitic therapy. The presence of the Herxheimer reaction is of further diagnostic significance if arsphenamine is used.

It is thought that in a certain percentage of the mild cases there is a hepatitis, while this is present in all cases of the severe form of the disease. It is important to determine early in the disease whether there is damage of the liver, because it is unwise to treat with the arsenicals a patient who has hepatitis, although it is equally important to use as strenuous treatment as is consistent with safety.

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7. Wile, U. J., and Karshner, R. G.: Icterus Gravis Syphiliticus and Its Relation to Acute Yellow Atrophy, J. A. M. A. **68**:1311 (May 5) 1917. Wile, U. J.: Syphilis of the Liver, Arch. Dermat. & Syph. **1**:139 (Feb.) 1920.

Investigators of recent years have added various tests of function of the liver, some of which are valuable in determining the degree and type of injury to the liver. The tests found most useful have been the estimation of dye excretion and the determination of the bilirubin content of the blood. Some of those who have used the phenoltetrachlorphthalein dye test in cases of syphilis either before or after treatment are Rosenthal,[8] Greenbaum and Brown,[9] Friedenwald,[10] Ottenberg, Rosenfeld and Goldsmith,[11] Berger,[12] O'Leary,[13] Silverman,[14] Piersol and Bockus,[15] Shattuck,[16] Shattuck, Browne and Preston.[17] More recently, Rosenthal and White [18] developed the bromsulphalein test, which has the same diagnostic importance as the phenoltetrachlorphthalein test; they claim that this dye is nontoxic. Epstein and Rauschkolb [19] used rose bengal as their test dye.

The tests with dye serum have not always proved of great value in determining the damage to the liver produced by syphilis. Friedenwald [10] stated that in syphilis of the liver, retention of the dye may or may not occur, depending largely on the degree of involvement. Ottenberg and others [20] showed that the test was positive in two cases of hereditary syphilis, but was negative in three cases of syphilis of the

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8. Rosenthal, S. M.: The Phenoltetrachlorphthalein Test for Hepatic Function, J. A. M. A. **83**:1049 (Oct. 4) 1924.

9. Greenbaum, S. S., and Brown, H.: The Phenoltetrachlorphthalein Liver Test, J. A. M. A. **82**:88 (Jan. 12) 1924.

10. Friedenwald, J., and Morgan, Z.: Some Observations on the Rosenthal Phenoltetrachlorphthalein Test as a Means of Determining Liver Function, Ann. Clin. Med. **4**:415 (Nov.) 1925.

11. Ottenberg, P.; Rosenfeld, S., and Goldsmith, L.: The Clinical Value of the Serum Tetrachlorphenolphthalein Test, Arch. Int. Med. **34**:206 (Aug.) 1924.

12. Berger, S. S.; Cohen, M. B., and Selman, J. J.: Liver Function Tests, J. A. M. A. **86**:1114 (April 10) 1926.

13. O'Leary, P. A.: Post Arsphenamine Jaundice, M. Clin. N. Amer. **8**:1203 (Jan.) 1925.

14. Silverman, D. N.: Phenoltetrachlorphthalein Test of Liver Function, New Orleans M. & S. J. **76**:333 (Jan.) 1924.

15. Piersol, G. N., and Bockus, H. L.: Comparative Studies in Liver Function, by Some of the Later Methods, J. A. M. A. **83**:1043 (Oct. 4) 1924.

16. Shattuck, H. F.: Clinical Use of Liver Function Tests; the Icterus Index and Rowntree-Rosenthal Serum Dye Test, M. Clin. N. Amer. **9**:601 (Nov.) 1925.

17. Shattuck, H. F.; Browne, J. C., and Preston, M.: Clinical Value of Some Recent Tests for Liver Function, Am. J. M. Sc. **170**:510 (Oct.) 1925.

18. Rosenthal, S. M., and White, E. C.: Clinical Application of the Bromsulphalein Test for Hepatic Function, J. A. M. A. **84**:1112 (April 11) 1925.

19. Epstein, N. N., and Rauschkolb, N. E.: The Rose-Bengal Test for Liver Function, Arch. Dermat. & Syph. **14**:122 (Aug.) 1926.

20. Ottenberg, R., and Abramson, H. A.: Production of Liver Necrosis by Tetrachlorphenolphthalein and Tetrabromphenolphthalein, J. A. M. A. **84**:800 (March 14) 1925.

liver in adults, the diagnosis in one of the cases being confirmed by laparotomy. Greenbaum and Brown,[9] on the other hand, found the dye test valuable in determining the action of the arsenicals on the function of the liver. Three of their six patients who had dermatitis following treatment showed retention of dye. Furthermore, in a large series of patients receiving a number of injections, only a small proportion showed dysfunction of the liver as indicated by the dye test.

A few observers have reported toxic reactions following the use of phenoltetrachlorphthalein. Maurer and Gatewood [21] reported three deaths following its use, while Ottenberg and Abramson demonstrated experimentally extensive lesions in the liver when overdoses of the drug were used. Bloom and Rosenau [22] concluded from their work that the use of this dye would produce a positive van den Bergh test in a normal person within sixty minutes. Twenty-two and two hundredths per cent of their patients who were tested showed a local reaction; 14.8 per cent developed thrombosis at the site of injection, and 7.4 per cent developed chills.

ESTIMATION OF BLOOD BILIRUBIN

Two methods for the estimation of bilirubin in the blood have led to numerous investigations and a voluminous literature on this subject during recent years.

Van den Bergh [23] made use of Ehrlich's diazo reaction in detecting variations in the bilirubin content of the blood serum. The color reaction depends on the formation of a reddish-purple azo dye, azobilirubin, when an acid solution of a diazonium salt is mixed with an alcoholic solution of bilirubin. Van den Bergh and Schnapper [24] made clinical use of this reaction in studying disease in which there was a variation from the normal amount of serum bilirubin. Van den Bergh noticed that in obstructive types of hyperbilirubinemia, the addition of the reagent alone to the serum produced a "direct reaction," and that it was not necessary to prepare the alcoholic solution of bilirubin from the blood serum to obtain this reaction. The bilirubin in the bile reacts in the same manner as the bilirubin of the blood stream in obstructive jaundice. The bilirubin found normally in small amounts in the blood serum and in greater amounts in certain hemolytic conditions reacted only when this protein

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21. Maurer, S., and Gatewood, L. C.: Phenoltetrachlorphthalein Liver Function Test, J. A. M. A. **84**:935 (March 28) 1925.

22. Bloom, W., and Rosenau, W. H.: The Reaction of the Liver to Phenoltetrachlorphthalein in Early Obstructive Jaundice, Arch. Int. Med. **34**:446 (Oct.) 1924.

23. Van den Bergh, H.: La récherche de la bilirubine dans le plasma sanguin par la méthode de la réaction diazoique, Presse méd. **29**:441 (June 4) 1921.

24. Van den Bergh and Schnapper, quoted by Ravdin, E. G.: Am. J. M. Sc. **169**:850, 1925.

bound bile pigment had been separated by alcoholic solution ("indirect reaction"). He also noted that a direct reaction was delayed in certain cases of nonobstructive jaundice. It seemed evident that bile pigment might exist in the serum in different forms. He concluded that the difference in reaction was due to some action the hepatic cells might have on the pigment, and that whenever the bilirubin of the serum gave the direct reaction, it was of the obstructive type.

In making a brief summary of the significance of these reactions, Vaughan,[25] Hagood [26] and others interpreted them as follows:

1. An immediate direct reaction indicates obstructive jaundice.

2. A delayed direct reaction suggests impaired hepatic function—injury of the liver cell or nonobstructive jaundice.

3. A direct negative reaction with a hyperbilirubinemia giving the indirect reaction only points to a nonobstructive jaundice of the hemolytic type.

With a marked increase of bilirubin in the blood, there is usually a positive reaction in all phases of the test.

By colorimetric methods, the test has been widely utilized for quantitative determinations, the indirect reaction in which all forms of bilirubin are measured as one being used.

Normal serums contain from 1 to 3 mg. of bilirubin per liter. On comparison with the standard which represents a concentration of 5 mg. per liter or one unit, normal serums may be said to range from 0.2 to 0.6 of a van den Bergh unit (Ravdin [27]). Schamberg and Brown [28] and O'Leary [13] used the quantitative method as a measure of damage to the liver during and after arsphenamine therapy.

THE ICTERUS INDEX

Meulengracht [29] devised a method for the direct estimation of the bilirubin content of the blood by colorimetric comparison of the fresh blood plasma to an arbitrary standard color similar to that of bilirubin—a 1:10,000 potassium dichromate solution. This method has been modified by Maue;[30] instead of plasma, the serum is used. A further

25. Vaughan, W. T.: Jaundice, J. Lab. & Clin. Med. **9**:210, 1923; Personal communication to the authors, February, 1926.

26. Hagood, D. S.: Liver Function and Liver Function Testing, M. Clin. N. Amer. **9**:1219 (Jan.) 1926.

27. Ravdin, E. G.: An Estimation of the Clinical Value of the van den Bergh Test, Am. J. M. Sc. **169**:850 (June) 1925.

28. Schamberg, J. F., and Brown, H.: Bilirubin Determinations in the Blood as a Measure of Liver Damage in Treatment with Arsphenamine, J. A. M. A. **82**:1911 (June 14) 1924.

29. Meulengracht, E.: Die klinische Bedeutung der Untersuchung auf Gallfarbstoff in Blutserum, Deutsches Arch. f. klin. Med. **132**:285 (July) 1920.

30. Maue, H. P.: Icterus Index of the Blood Serum, Surg. Gynec. Obst. **34**: 752 (June) 1922.

modification was made by Killian,[31] who substituted a fixed standard in the form of a colored glass disk.[32] The relative intensity of the color of the blood serum as compared to the arbitrary standard may be expressed numerically, and this color numerically expressed is known as the "icterus index."

The standard is taken as having a numerical index of 15. Normal serums have indexes of from 3.5 to 6, St. George's [33] average index of 120 control cases being 4.41 with a range from 2 to 9, 90.8 per cent being between 3.5 and 5.5. Clinical icterus is present with an index above 15, while it is absent with an index below this figure. Between the upper limit of normal and the point of clinical icterus is a zone of latent icterus. Bernheim,[34] St. George and Brown,[33] Barrow, Armstrong and Olds,[35] Shattuck,[16] Shattuck, Browne and Preston,[17] and Chargin and Orgel [36] presented a large number of clinical cases wherein the icterus index was determined, and they have made valuable contributions toward interpreting the value of this test. Shattuck regarded the icterus index as the most useful clinical method of studying the function of the liver. Bernheim said that it is an accurate method for determining the degree of bilirubinemia, and technical sources of error are readily controlled. Barrow regarded it as the test of choice among those in use. St. George regarded the quantitative van den Bergh test as slightly more accurate, but thinks that for ordinary clinical purposes the test is needlessly complex of performance. Perhaps with the use of the fixed Killian glass standard, his experience, like ours, would have been that the icterus index was the more accurate of the two. We have also found that one of the most disturbing sources of error, i. e., the hemolysis produced during collection of blood and the obtaining of serum, can be avoided by the use of the Keidel vacuum tube.

Hess and Myers [37] and Bernheim [34] called attention to the false color in the serum which may occasionally be produced by certain articles of diet, and we have learned that a specimen of blood obtained shortly after a meal is apt to be chylous; this condition interferes with colorimetric

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31. Killian, G. A.: An Improved Colorimeter, J. Lab. & Clin. Med. **10**:570, 1925.

32. This is supplied, together with Killian's colorimeter by the Klett Manufacturing Company, New York.

33. St. George, A. V., and Brown, A. L.: The Value of the Icterus Index in Differentiating Anemia, Arch. Int. Med. **36**:847 (Dec.) 1925.

34. Bernheim, A. R.: The Icterus Index, J. A. M. A. **82**:291 (Jan. 26) 1924.

35. Barrow, J. V.; Armstrong, E. L., and Olds, W. H.: Further Clinical and Operative Studies of the Icterus Index, Am. J. M. Sc. **170**:519 (April) 1925.

36. Chargin, L., and Orgel, S. Z.: Jaundice in Syphilitic Persons Receiving Arsenical Medication, Arch. Dermat. & Syph. **7**:495 (April) 1923.

37. Hess, A. F., and Myers, V. C.: Carotinemia, J. A. M. A. **73**:1743 (Dec. 6) 1919.

readings. In the few cases in which this may occur, the reading is only slightly higher. Both of these possible sources of error may be controlled by obtaining the blood specimen during the fasting state.

It is not our present intention to be concerned with the derivation of bile pigment, but, since the liver is the chief excretory organ of this substance, the estimation of the amount and kind of bilirubin in the blood is taken as an estimate of a disturbance in this function of the liver.

We have adopted the icterus index as a quantitative estimate of the bilirubin in the blood and have used the van den Bergh test qualitatively to determine the type of jaundice.

REPORT OF A CASE

A white man, aged 25, single, American, was referred to us because he had a positive blood Wassermann reaction and a severe jaundice. About two months before, a small sore had developed on his penis following frequent exposures. The lesion was not painful, but somewhat indurated. He did not consult a physician, but used powders locally. One month after its appearance, the lesion healed; about this time he had daily attacks of nausea, which were followed by vomiting. This condition occurred after meals and lasted for four or five days. He then noticed that his skin was becoming yellow; this condition gradually became more pronounced. He felt weak and generally below par. At night, he felt as though he had a rise in temperature; however this was not verified, as his temperature was not taken. For the past three weeks he had had slight dizziness at times, but had been free from headaches. The appetite had been poor, and he had lost about 10 pounds (4.5 Kg.) in weight. He was constipated. For a week before he consulted us, he had slept poorly. He complained of pain in the shoulder and back, extending to the left side of the neck. Three Lyon's nonsurgical biliary drainages had been performed and had been followed by a progressive increase in the jaundice. At the beginning of this treatment, while the patient was under the care of an internist, the icterus index was 45. The patient had had two negative blood Wassermann reactions in our laboratory during the previous year.

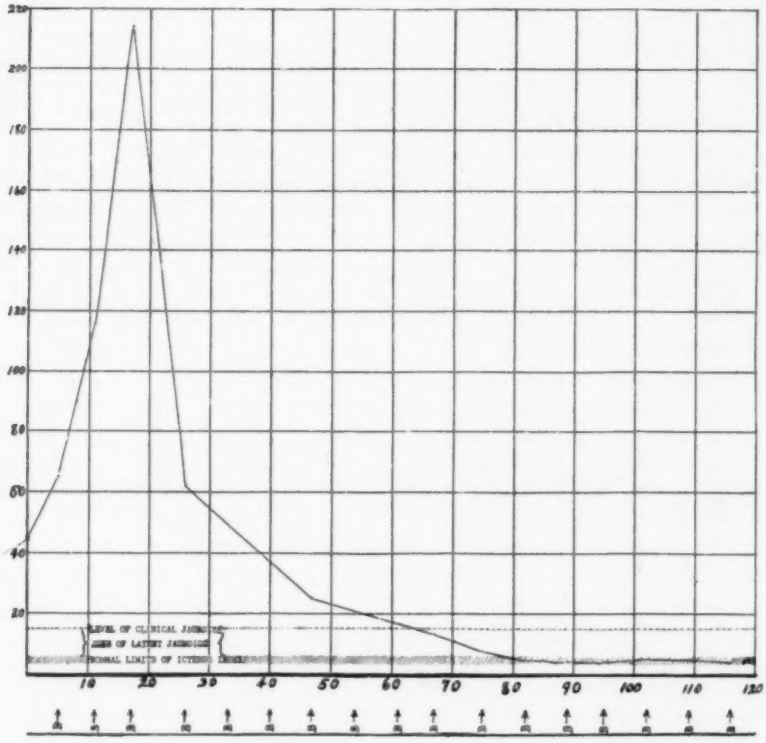
Examination.—Exa.nination revealed a fairly well nourished man of toxic appearance. The eyes were sunken; the pupils were equal and reacted to both light and in accommodation. The skin was deeply icteric. The mucous membranes were markedly icteric, and mucous patches were not apparent. There was a moderate generalized enlargement of the lymph glands. A few papular lesions were scattered over the trunk. At the urinary meatus, there was an indurated involuting lesion. Results of examination of the bones, heart and lungs were negative. The pulse rate was 72 and the temperature was normal. The liver was felt two fingerbreadths below the costal margin and was tender. The spleen was not palpable. The tendon reflexes were normal.

Laboratory Examination.—The feces were pale but otherwise normal. The urine was alkaline; its specific gravity was 1.018. Urinalysis revealed: albumin, faint trace; no sugar; test for bile, strongly positive; test for urobilinogen, positive; no casts, pus or blood; urate crystals; no leucin or tyrosin crystals.

Examination of the blood revealed: white blood cells, 7,300; polymorphonuclears, 66 per cent; lymphocytes, 28 per cent; large mononuclears and transitionals, 5 per cent; eosinophils, 1 per cent; red blood cells, 5,500,000.

On account of hyperbilirubinemia it was impossible to read the hemoglobin content by the Newcomer method, estimated by the Tallquist method at 90 per cent. The Wassermann reaction was strongly positive (++++). Bilirubin determinations showed: icterus index, 65; qualitative van den Bergh test: direct immediate, negative; delayed, strongly positive; indirect, strongly positive.

Diagnosis.—The diagnosis of early syphilis was established by the fact that the patient had an involuting primary sore and a strongly positive Wassermann reaction. There were records of two negative Wassermann reactions



Curve of icterus indexes of case reported. Ordinates represent quantitative blood bilirubin determinations as icterus indexes. Abscissae represent days of observation. *B*, represents 0.1 Gm. amounts of potassium bismuth tartrate given intramuscularly.

during the year prior to his present illness. It was assumed that the jaundice was syphilitic in origin because he had had early syphilis, and because the jaundice became worse in spite of repeated nonsurgical biliary drainages. The progressive jaundice, loss of strength and weight, nausea and vomiting, constipation, muscular pains and severely ill appearance strongly suggested an early stage of a grave icterus. In addition to the clinical features, there was laboratory evidence of injury to the hepatic cells, as indicated by the negative direct immediate and the positive direct delayed van den Bergh reactions.

Treatment and Progress.—Due to the severity of the liver disturbance, bismuth was the drug of choice in the treatment, and it was given in 0.1 Gm. doses at weekly intervals. Six days following the first injection of bismuth, the patient's symptoms seemed more grave. The liver was larger and more tender, and there was additional loss in weight. The blood bilirubin determinations showed an icterus index of 116, and the van den Bergh test was now strongly positive in all phases. The patient was given a second injection of bismuth, and during the subsequent six days he became progressively worse, and his icterus index was 214. At this time, the patient's eyes were sunken, there was further reduction in weight (25 pounds [11.3 Kg.] below normal), weakness was greater, the liver was still enlarged and tender, and the intense bronzing jaundice gave an alarming appearance. Following the third treatment, the patient began to improve rapidly, both subjectively and objectively, the icterus index being 62 nine days following the treatment. The patient's condition rapidly improved, and within the next three weeks' during which time three more injections of bismuth had been given, the icterus index declined to 25 and the van den Bergh test still showed a definitely positive direct delayed reaction while the immediate reaction was negative. Clinically the jaundice, though greatly lessened, was still present. There was a rapid gain in weight and strength, and the liver was not palpable. Three weeks later, the index was 13.6; clinical jaundice had disappeared. Within the next two weeks, the index became a normal 5 and remained within normal limits. To date, he has received twenty injections, and he says that he feels as well as ever. He has regained his normal weight.

COMMENT

In the diagnosis and as a guide to the treatment in this case, we found the icterus index and the van den Bergh test of great value. The icterus index was taken as the quantitative estimate of the bilirubin content of the blood, while the qualitative van den Bergh test was used to determine the type of jaundice. The latter test indicated that in the earlier stages of this case, the jaundice was due to injury of the hepatic cells.

In twenty-five control cases of early syphilis, a study was made by means of both tests to determine, first, the effect of early syphilis and, secondly, the effect of treatment on the liver function as indicated by the bilirubin content of the blood. Aside from the case reported here we found normal blood bilirubin in all cases on entrance examination. The blood of all except three patients was normal for bilirubin throughout the treatment; the amount of drugs given varied, some patients receiving as many as twenty injections of neoarsphenamine and from fifty to sixty injections of bismuth.

The three patients who showed a slight increase in the bilirubin content of the blood were receiving neoarsphenamine according to Ormsby's [38] method, bismuth being administered between courses. The first of these had received five treatments with neoarsphenamine and five

38. Ormsby, O. S.: A Valuable Method of Employing Arsphenamine in Syphilis, J. A. M. A. **75:1** (July 3) 1920.

injections of bismuth. Seven determinations of the bilirubin of the blood of this patient showed a normal content. Two days following the fifth injection of neoarsphenamine, the icterus index was 7.1 and the van den Bergh test showed an increase in the indirect reaction pointing only to a hemolytic process. Tests of the other two patients showed indexes of 9.3 and 8.8, both following the third injection of neoarsphenamine. In both of these, the van den Bergh test indicated hemolysis. All of these reactions indicated only a slight increase of bilirubin, and since there were no other clinical signs, and since the reactions did not persist even with further treatment, they were of minor significance.

In this small control group, liver damage following treatment was not appreciable. This agrees with the observations made by Schamberg and Brown [28] with the van den Bergh test and those of Greenbaum and Brown [9] with the Rosenthal test of dye excretion.

In this series of cases, we used Ehrlich's urobilinogen test of the urine, and we agree with Brown and Greenbaum [39] that the results are too variable to serve as an index of hepatic damage.

CONCLUSIONS

1. A case of the rare condition, early syphilitic hepatitis, is reported.

2. The icterus index determination and the van den Bergh test are most useful methods for determining liver dysfunction produced by early syphilis.

3. The icterus index as a quantitative estimation of blood bilirubin and the van den Bergh test as a qualitative reaction are distinct aids in diagnosis and should be used as guides to treatment.

4. Twenty-five control cases of early syphilis did not show any increase in the blood bilirubin before treatment. Twenty-two of these remained normal throughout treatment; the three remaining cases showed a blood bilirubin content slightly above the upper limit of normal at one time during treatment.

5. Treatment with bismuth has proved to be of great value in a case of early syphilitic hepatitis.

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39. Brown, H., and Greenbaum, S. S.: Urobilinogen Determinations in Treated Syphilitic Patients, Arch. Dermat. & Syph. **14**:434 (Oct.) 1926.

ACUTE SYPHILITIC PHLEBITIS*

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Recently it has been our privilege to observe a patient in the secondary stage of syphilis who presented a phlebitis of the superficial veins of the lower extremities. Syphilitic phlebitis is one of the unusual manifestations of the disease, the veins seeming to enjoy a comparative immunity. This fact is in striking contrast to the arterial side of the vascular bed which is so frequently attacked by the spirochete.

The first clinical observations on acute syphilitic phlebitis were recorded in 1860 by Girwood,[1] who noted the occurrence of a peculiar phlebitis of the superficial veins of the lower extremities in three young men suffering with syphilis in its early secondary period. Since that time, French and German syphilographers have studied the condition from both a clinical and a pathologic standpoint. In 1903, Roussy[2] was able to collect the reports of thirty-five observations in the literature, including two of his own. Since 1903, probably not more than twenty-five reports on the various syphilitic phlebitides have appeared. We were unable to find a single report in the literature concerning acute syphilitic phlebitis by American authors. Likewise, our textbooks have meager descriptions of the condition.

REVIEW OF THE LITERATURE

A review of forty-five reported observations of the various syphilitic phlebitides is sufficient to give the information desired, although this is not the total number to be found. For convenience, we have arranged the data into three tables. Table 1 contains only those cases in which the superficial veins have been involved early in the disease, usually coincident with the appearance of the secondary eruption. Table 2 shows those cases in which the phlebitis manifests itself as subcutaneous nodes along the course of the veins of the hypoderm. Table 3 deals with those cases in which phlebitis develops several years after the initial infection.

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* Read at the Fiftieth Annual Meeting of the American Dermatological Association, May, 1927.

1. Girwood, C. P.: On Three Cases of Phlebitis Occurring in Patients Affected with the Syphilitic Poison, Lancet **1**:619, 1860.

2. Roussy, G.: Phlébite syphilitique secondaire, Gaz. d. hôp. **76**:1013, 1903.

TABLE 1.—*Reports of Early Syphilitic Phlebitis in the Literature*

Author	Age	Sex*	Occupation	Duration of the Infection	Veins Affected	
Girwood (Lancet **1**: 619 1869)	..	♂	.....	Secondaries	Left leg; superficial veins	Recurrence
	..	♂	.....	2 months	Left leg, then right leg	Recurrence
	..	♂	.....	Secondaries	Left leg, then right leg	Recurrence
Gosselin (Clinique de la charite **1**: 612, 1873. Cited by Mendel)	25	♀	.....	Roseola	Left leg (thigh)	
	25	♂	.....	3½ months	Both legs	
Gayraud (Gaz. hebd. des sc. med. de Montpelier, 1883, no. 43. Cited by Mendel)	31	♂	Tanner	3 months	Left leg; internal saphenous to its femoral opening	
	23	♂	.....	Secondaries	Bacilic vein	
Cautru (France Med., January, 1882. Cited by Mendel)	22	♂	Newspaperman	Secondaries	Each thigh	
Breda (Revista veneta si scienze mediche, in Thèse Collinot, 1889, p. 63)	28	♀	.....	Secondaries	Both arms and legs	
Mauriac (Leçons sur la syphilis tertiare et hereditaire, 1890, p. 883. Cited by Mendel)	20	♂	.....	2 months	Right leg, then right arm, then left leg	Recurrence
Fournier (Traite de la syphilis, vol. 1, p. 705. Cited by Mendel)	..	♂	.....	Secondaries	Basilic vein	
Mendel (Arch. gen. de med. **1**: 292, 1894)	22	♂	.....	1 month	Both legs and arms	Recurrences
Fournier and Loeper (Bull. et soc. franc. de dermat. et syph. **10**: 42, 1899)	40	♂	.....	Secondaries	Both legs and arms (progressing from one to other)	
	22	♂	.....	Secondaries	Both legs, then both arms	
LeNoir (Assoc. franç. pour l'avance d. sc. C.-r., 1899, Paris, 1900, vol. 28, part 2, p. 703)	..	♂	Policeman	3 months	Left leg	
	23	♀	Servant	12 days, roseola	Left leg, then both legs	Recurrence
Jacquinet (Union méd. du nord-est **24**: 253, 1900)	30	♂	.....	3 months	Right calf	
Campbell (Bull. et mém. Soc. méd. d. hôp. de Paris **19**: 1005, 1902)	38	♂	Brick mason	10 months	Right thigh, then internal saphenous right leg (patient was at rest; hemiplegia, right)	Recurrence
Hoffman (Dermat. Ztschr. **10**: 470, 1903)	36	♂	Builder	2 months	Left leg (points resemblance to erythema nodosum)	
	22	♂	Seaman	2 months	Right leg, then left	
Roussy (Gaz. d. hôp. **76**: 1013, 1903)	26	♂	.....	Secondaries	Both internal saphenous	
	25	♂	Brick mason	5 months	Both internal and external saphenous	
Renault and Roussy (Bull. et mém. Soc. méd. d. hôp. de Paris **20**: 100, 1903)	29	♂	Wheelbarrower	2 months	Both legs (progressive)	
Tourneux and Levy (Toulouse méd **10**: 49, 1908)	32	♂	Wood carver	2 months	Internal saphenous	
Thibierge and Ravaut (Bull. et mém. Soc. méd d. hôp. de Paris **29**: 342, 1910)	29	♂	Waiter	2 months	Right thigh, then arms and legs (progressive), demonstrated spirochetes	
Strandberg (Arch. f. Dermat. u. Syph. **107**: 187, 1911)	32	♂	.....	Roseola	Left leg	
	20	♂	.....	Roseola	Both legs	
Tourneux (Arch. méd. de Toulouse **19**: 381, 1912)	33	♂	Waiter	Secondaries	Left leg, then right	
Achard and Demanche (Arch. d. mal. du coeur **2**: 449, 1909)	..	♂	.....	Secondaries	Ieft leg and less on right (deep veins with edema; also nephritis, syphilitic)	
Balzer and Vandexneveux (Bull. soc. franç. de dermat. et syph. **21**: 141, 1910)	22	♀	.....	Secondaries	Saphenous, basilic and cephalic veins; also nodules	
Frieboes (Dermat. Ztschr. **20**: 125, 1913)	..	♂	.....	5 months	Indurated cord in each temporal fossa	
Versé (Beitr. z. path. Anat. u. z. allg. Path. **56**: 580, 1913)	19	♂	Student	10 months	Patient died after a stormy course; cerebrospinal veins found thrombosed at autopsy	

* In this table and in tables 2 and 3, ♂ indicates male and ♀, female.

TABLE 2.—*Reports of Nodular Thrombophlebitis (Early) in the Literature*

Author	Age	Sex	Occupation	Duration of the Infection	Veins Affected
Mendel (Arch. gen. de méd. **1**: 292, 1894)	47	♂	Sculptor	5 months	From five to six subcutaneous nodules along veins of forearm
Neisser (Berl. klin. Wchnschr. **40**: 377, 1903)	30	♂	Laborer	.....	Lentil sized subcutaneous nodes; (phlebitis migrans), biopsy
Gaucher et al. (Bull. et mém.Soc. méd. d. hôp. de Paris **20**: 119, 1903)	27	♀	.....	Early secondaries	Nodes in right cubital fossae
Balzer et al. (Bull. soc. franç. de dermat. et syph. **21**: 141, 1910)	22	♀	.....	2 months	Nodes along right cephalic vein and also veins of legs (both types)
Strandberg (Arch. f. Dermat. u. Syph. **107**: 187, 1911)	56	♀	Maid	Early secondaries	Nodes along superficial veins of arms and legs
Frieboes (Dermat. Ztschr. **20**: 125, 1913)	..	♂	Buyer	6 years	Nodes along facial veins of upper one-half of face
	42	♂	.....	Late	Subcutaneous nodes over forehead and temples

TABLE 3.—*Reports of Late Syphilitic Phlebitis in the Literature*

Author	Age	Sex	Occupation	Duration of the Infection	Veins Affected
Greenhow (Tr. Clin. Soc. London **6**: 143, 1873; cited by Mendel)	33	♂	.....	7 years	Superficial veins of legs
Langenbeck (cited by Mendel)	53	♀	.....	.....	Large gummatous mass attached to right external jugular
	42	♀	.....	4 years	Large gummatous mass attached to left femoral
Tourneux (Arch. méd. de Toulouse **19**: 381, 1912)	26	♂	.....	3 years	Questionable whether syphilitic phlebitis; autopsy: syphilis of liver with phlebitis of portal vein
Gaujard (Internat. Clin. **3**: 61, 1920)	50	♀	.....	30 years	Right arm; very edematous
	36	♂	.....	7 years	Right arm; very edematous
Manouelian (Surg. Gynec. Obst. **3**: 407, 1921)	..	..	.....	Congenital	Umbilical veins

From a study of these tables, the various phlebitides can be easily classified and the cases fall naturally into two groups, namely: those in which phlebitis develops within a few months of the onset of the infection and those in which phlebitis develops late in the course of the disease. In the first group, that is, early syphilitic phlebitis, there are two main varieties, the most common type being an involvement of the superficial veins of the extremities with the formation of indurated cords along their course. The other type manifests itself as nodules varying in size from that of a lentil to that of a pea; these nodules are attached to the superficial veins of the hypoderm. Rarely, the deep veins of the extremities or other portions of the body may be involved, as seen in the reports of Achard [3] and of Versé.[4]

In the second group of cases, that is, late syphilitic phlebitis, the deep veins of the extremities are usually affected, although rarely the superficial veins may be involved.[5] Occasionally gummatous masses develop about a vein, and it thus becomes secondarily affected. The late syphilitic phlebitides are much more rare than the early type.

In this report, we will confine our comment to the first type of case, that is, early syphilitic phlebitis with the development of indurated cords along the course of the superficial veins of the lower extremities.

Early syphilitic phlebitis may manifest itself as an inflammatory process involving the whole of a superficial vein, several segments of the vein, or a single segment. It has a tendency to be multiple, involving the veins of more than one limb and frequently progressing from one vein to another. The lower limbs are most frequently affected, the internal saphenous vein usually being attacked. This type of phlebitis is the most common variety of the syphilitic phlebitides, forming 72 per cent of the cases studied in the literature.

The phlebitis develops within a few months after the appearance of the initial sore, usually accompanying the early secondary eruption. Frequently the chancre is still present, and occasionally the phlebitis may precede the onset of secondary symptoms, as in the case reported by LeNoir.[6] The condition developed in a patient ten months after the primary lesion.[7] The severity of the infection does not seem to play a

3. Achard, C., and Demanche, R.: Phlébite syphalitique, Arch. d. mal. du coeur **2**:449, 1909.

4. Versé, M.: Ueber Phlebitis syphilitica cerebrospinalis, Beitr. z. path. Anat. u. z. allg. Path. **56**:580, 1913.

5. Greenhow: Tr. Clin. Soc. London **6**:143, 1873. Cited by Mendel: Arch. gen. de méd. **1**:292, 1894.

6. LeNoir: Deux cas de phlébite des membres observés dans la période secondaire de la syphilis, Assoc. franç. pour l'avance. d. sc. C.-r. 1899, Paris, 1900, vol. 28, pt. 2, p. 703.

7. Campell, C. M.: Un cas de phlébite syphilitique secondaire, Bull. et mém. Soc. méd. d. hôp. de Paris **19**: 1005, 1902.

part in the development of the phlebitis, although complications have been reported by several authors, such as a syphilitic nephritis, hemiplegia or arthritis.

SYMPTOMS

The symptoms are usually so slight that the condition may readily be overlooked, or they may be quite severe, causing the patient nocturnal pains, interfering with the use of the limb and keeping him from his usual occupation. There may be little constitutional reaction, or the process may be accompanied by a slight rise in temperature and moderate leukocytosis.

Over the vein or portion of the vein affected there is usually a reddening of the skin and occasionally local edema of the tissues. This acute reaction tends to subside spontaneously in a few days, when an indurated cord along the course of the vein can be felt, which is slightly tender. The limb affected may be slightly swollen but does not pit on pressure. Early syphilitic phlebitis has a remarkable tendency to recur either in the original vein affected, in another vein, or in another limb. In eight of the cases studied there was a definite recurrence of the condition, as well as in our case in which the recurrence took place, when the patient resumed his work while still under treatment. The process seems to require the same length of time to involute whether it is the original phlebitis or a recurrence. Prior to the time of arsphenamine therapy, the condition would clear in from five to eight weeks, but under the present antisyphilitic therapy involution is much more rapid, occurring in from two to three weeks.

The complications of syphilitic phlebitis are negligible, the vein returning to normal after the process clears. Embolus is unusual, Julien [8] reporting the single instance.

ETIOLOGY

Early syphilitic phlebitis is usually seen in the young adult but may occur at any age at which the infection is contracted. It is much more common in the male than in the female. Of the thirty-one cases noted in the literature, twenty-seven were in males and four in females, the ratio being about 7 : 1. Undoubtedly, the strain of occupation has some bearing on this fact. The phlebitis is usually seen in persons who stand up most of the day or whose occupation necessitates marked use of the limbs. A case is reported by Campbell [7] in which the phlebitis occurred in a patient who was at rest in bed, but it appeared on the same side as his hemiplegia.

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8. Julien: Les phlébite de la syphilis acquise, Internat. dermat. Kong. Verhandl. u. Ber. **2**:225, 1905; cited by Gaujard: Syphilitic Phlebitides, Internat Clin. **3**:61, 1920.

Alcoholism is said to be a contributing factor. It will be noted that, in the case report given, the patient is a blacksmith whose work it is to handle the levers on a large steam hammer. He stated that with each blow of the hammer his legs received a secondary shock, and it is of interest to note that he had been drinking heavily of wine and whisky previous to the onset of his phlebitis.

Varicose veins do not predispose to the condition.

PATHOLOGY

Thibierge and Ravaut [9] studied the microscopic changes of acute syphilitic phlebitis in 1910 and were the first to demonstrate *Spirochaeta pallida* in the lesions. They showed that there is little change in the endothelial layer of the vein and that the main pathologic change is a proliferation of connective tissue in the subendothelial layer which causes the endothelium to protrude into the lumen of the vein in the form of buds, thus narrowing the lumen. The presence of a clot is inconstant but, when it is present, it is usually adherent to the vein wall. There is no tendency for lymphocytic infiltration about the vasa vasorum.

Thibierge and Ravaut [9] also reproduced experimental syphilitic lesions by the inoculation of a small piece of the excised vein in the cornea of the monkey.

DIAGNOSIS

Early syphilitic phlebitis presents a clinical picture distinct from the phlebitis of other infectious processes. The main points of distinction are, first, the lack of constitutional and local symptoms; second, the multiplicity of veins involved; third, the marked tendency for syphilitic phlebitis to recur; fourth, the lack of formation of an embolus which is most unusual in syphilis while it is common in the other types, and fifth, the prompt response to specific therapy.

The lesions may simulate erythema nodosum rather closely, and Hoffmann [10] referred to his cases as erythema nodosa syphilitica. The diagnosis is readily made by finding other evidences of the disease and by its prompt response to antisyphilitic therapy.

TREATMENT

The reaction to arsphenamine is prompt, the condition subsiding within a few days. Although embolus is a rare complication, the

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9. Thibierge, G., and Ravaut, P.: Phlébites syphilitique secondaires multiples des membres; demonstration de la présence du spirochéte dans la paroi veineuse par l'examen microscopique et par l'inoculation experimentale du singe, Bull. et mém. Soc. méd. d. hôp. de Paris **29**:342, 1910.

10. Hoffmann, E.: Ueber strangförmige Phlebitis im Frühstadium der syphilis, Dermat. Ztschr. **10**:479, 1903.

patient should be at rest in bed with the affected member elevated and hot compresses applied to it.

REPORT OF CASE

History.—F. R., an Italian blacksmith, aged 30, referred by Dr. Mark Lessard, entered the night syphilis clinic of the University of California on Sept. 20, 1926, complaining of pain and swelling of the right leg and of swelling of the right side of the face. The family history was unessential.

Three years previously, the patient had a tonsillectomy performed which was followed by a chronic enlargement of the lymph nodes under the right angle of the jaw.

He had been drinking from a half to one gallon of wine daily for the past three months with whisky occasionally. He said that he had been chronically intoxicated throughout this period.

As the man was a blacksmith, his work was hard and necessitated the use of a steam hammer all day. With each blow of the hammer, there was a secondary shock felt in the lower limbs.

He had had gonorrheal infections five years and one year before admission. Otherwise, the past history was unessential.

Two and a half months previously, the patient developed a sore at the sulcus of the penis which had followed exposure two and one-half weeks. The sore had been treated with cautery and a white powder locally and had healed in about ten days. The patient felt well until about one month prior to entry, when he noticed that the inguinal glands became enlarged bilaterally, and at the same time he began to suffer with general malaise and severe headache. This persisted for two weeks.

About two and one-half weeks previous to entry, the patient began to suffer with pain in the left calf which caused him to stop work. The left ankle was slightly swollen. The discomfort in this leg began to subside with a coincident development of pain in the right calf, which definitely impeded locomotion. At this time, the right side of the patient's face became more swollen than usual and slightly tender. Generally, the patient felt fairly good except for the discomfort in his legs and right jaw.

Physical Examination.—The man was well developed and well nourished and complained of his right leg. The examination revealed nothing of importance except the following:

(1) An enlargement of the right side of the face and neck, obliterating the right angle of the jaw and forming a mass the size of an orange. The swelling over the face corresponded to the outline of the right parotid gland but it fused with the mass in the neck which could not be distinguished from the lymph nodes. The mass was slightly tender to palpation. This was later found to be a separate and unrelated condition.

(2) A faint generalized roseola, most marked over the sides of the body.

(3) Marked enlargement of the inguinal nodes, which were discrete and not tender, and general lymphadenopathy.

(4) Scar on penis in sulcus.

(5) Slight enlargement of the right calf and swelling of the right ankle which did not pit on pressure. There was a moderate tenderness over the midcentral portion of the calf which extended about 10 cm. in a linear direction. A diffuse mass could be made out but no cord. The skin over this mass was dull red. The left calf in its lower third was also tender, but no mass or cord could be made out.

The temperature was not taken at the first visit.

Laboratory Examination.—The results of the Kolmer modification of the Wassermann reaction were: with 0.1 dilution of the patient's blood serum, +++; with 0.02, ++++; with 0.004, ++; with 0.002, — and with 0.001, —.

Examination of the spinal fluid showed: a negative Wassermann reaction with 0.1, 0.02, 0.004, 0.002 and 0.001 dilutions of the patient's serum; cell count: 3 mononuclears; the colloidal gold curve, 0011000000; protein, normal; globulin, negative.

The urine showed: albumin, 0; sugar, 0; specific gravity, 1.026. Microscopically, the urine was negative.

Examination of the blood showed: hemoglobin, 60 (Sahli); red blood cells, 3,560,000; white blood cells, 9,400. The differential count was normal.

Diagnosis.—The condition was diagnosed as early syphilis—secondary stage, with phlebitis of the internal saphenous vein of each leg.

Course.—On Sept. 21, 1926, at 10 a. m., 0.6 Gm. of neoarsphenamine was given intravenously. At 9 p. m., the patient showed a typical Herxheimer reaction. The previously hardly perceptible roseola had become markedly intensified. The patient had a mild diarrhea and had had four bowel movements since 3 p. m. He felt sick and feverish. The condition of the legs was about the same.

On September 22, the patient felt well. The eruption had almost completely faded. The right leg felt much better and was not so tender.

On September 25, the patient felt "fine." Eruption was not present. The legs were much better and were not tender. A cord could not be made out. Arsphenamine, 0.4 Gm., was given intravenously.

On September 27, the patient returned to work.

On September 30, the patient was seen at his hotel. There had been a recurrence of symptoms following his return to work. With each strain at his work he would feel sharp pain in the right calf, which became so severe that he had to stop.

Examination showed that the right leg was slightly swollen, with reddening of the central portion of the calf in an area about 4 by 10 cm. large. A hard cord, slightly tender, about the size of the index finger and extending 10 cm. along the center of the calf could be felt. On the anterior surface of the right leg could be seen three areas of erythema, each about the size of a half dollar, which were tender on pressure. There was slight edema of the right ankle, which did not pit on pressure.

On October 1, 0.4 Gm. of arsphenamine was given intravenously. The patient entered the University Hospital.

Examination in the Hospital.—The temperature on entry was 38.2 C. (100.7 F.). It was normal on the following day. The systolic blood pressure was 120; diastolic, 78. The reflexes were normal.

On October 2, the blood count showed: hemoglobin, 80 per cent (Sahli); red blood cells, 4,720,000; white blood cells, 10,000; polymorphonuclears, 73 per cent; lymphocytes, 25 per cent; transitionals, 2 per cent. The red cells appeared normal in smear. The platelets were normal in number.

Examination of the urine showed: specific gravity, 1.026; clear; albumin, 0; sugar, 0; occasional white blood cell; urobilin, 0; bile, 0.

Examination of the stool gave negative results.

On October 5, 0.3 Gm. of arsphenamine was given intravenously. A mild nitritoid reaction occurred, followed by a chill lasting five minutes. The leg was much better. The erythematous areas on the anterior surface of the right leg had disappeared, leaving shotlike, freely movable, slightly tender masses under the skin. The cord in the right calf was smaller and less tender.

On October 12, 0.2 Gm. of asphenamine was given intravenously. A severe nitritoid reaction, with a chill lasting twenty-five minutes occurred. The right leg continued to improve.

On October 18, 1½ grains (0.09 Gm.) of mercury salicylate was given intragluteally.

The cord in the right calf could be made out with difficulty. Tenderness was not present. The patient went back at work and did not have further pain. He felt fine.

On October 22, the cord in the right calf had disappeared entirely.

On October 25, a second recurrence took place. The patient noticed a tender nodule behind the right knee. On that day, he had been doing heavy lifting. Following the application of hot compresses and rest, the swelling diminished in size but the area remained tender.

Examination.—A nodule about 2.5 by 1 cm. was present in the right popliteal space, which was firm and slightly tender. Changes in the skin were not present, nor was there any edema of the legs.

On November 2, the nodule under the right knee had subsided markedly. One grain (0.06 Gm.) of mercuric chloride was given intragluteally.

On November 9, the patient felt well. Nodules were not present. The legs were normal.

The patient has been under continuous antisyphilitic therapy, having tolerated neoarsphenamine, and has not had further trouble from the phlebitis.

COMMENT

This case is a classic example of early syphilitic phlebitis. The phlebitis came on during the fourth month of the infection, beginning in the left calf and later appearing in the right calf as the first lesion subsided. The patient improved markedly under treatment with arsphenamine, but the condition recurred when he resumed his work. A second, but milder, recurrence developed later. The patient's occupation and alcoholic tendencies were predisposing factors in the production of the phlebitis.

The involvement of the small venules over the surface of the right leg, as shown by the three areas of erythema described during the first recurrence, is unusual as we have not found a description of such a condition in the cases studied.

384 Post Street.

THE RELIABILITY OF THE KOLMER-WASSERMANN REACTION IN PREGNANCY*

ARTHUR WILLIAM STILLIANS, M.D.
CHICAGO

Since the early days of the Wassermann reaction, the possibility of false positive results has been recognized as of the utmost importance. Among nonsyphilitic conditions cited as productive of such misleading results, Grosz and Bunzel,[1] in 1909, reported temporary positive tests during eclamptic seizures. Since then, the danger of false positive reactions not only in eclamptic persons but in healthy women during the latter months of pregnancy has been emphasized. Until only a few years ago a number of authors advocated that routine serologic examination of pregnant women be abolished as its value was too uncertain and as it put a needless financial drain on obstetric clinics and caused unnecessary worry to patients and their families.[2]

False positive reactions are possible in any serologic laboratory, but they occur rarely, I believe, in those using the Kolmer technic. It is reasonable to expect them more frequently in serum from the pregnant woman than in other serums. However, the estimate of Belding[3] that "as high as 25 per cent of the positives in pregnant women with cholesterolized antigens may prove non-syphilitic" is, in my opinion, much too high for the Kolmer-Wassermann reactions. Weakly positive reactions fluctuating to negative and back to weak or even strong positive are so common in old syphilitic patients that it is only reasonable to expect them to occur in a certain percentage of pregnant syphilitic women; but, in itself, this is not evidence of false positive reactions. Women infected with syphilis develop resistance better than men; the manifestations are fewer and milder, and in them the disease becomes latent earlier. Pregnancy accentuates this tendency and is in itself a treatment of syphilis,[4] so much so that it reduces the danger of syphilis

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* Read at the Fiftieth Annual Meeting of the American Dermatological Association, May 12 to 14, 1927.

* From the Serological Laboratory of the Chicago Lying-In Hospital.

1. Grosz and Bunzel: Ueber das Vorkommen lezithinausflockender und komplementbindender Substanzen im Blute Eklamptischer, Wien. klin. Wchnschr., 1909, p. 783.

2. Stuhmer, A., and Dreyer, K.: Unreliability of Serum Examinations for Syphilis in Pregnancy and Parturition, Ztschr.f.Geburtsh.u.Gynäk. **84**:289, 1921.

3. Belding, D. L.: The Wassermann Test, Am. J. Obst. & Gynec. **9**:203 (Feb.) 1925.

4. Stokes, John H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Co., 1926, p. 24.

of the central nervous system.[5] Thus, the probability that syphilis will be revealed by clinical evidence is considerably less in the woman who has gone through pregnancy than in other women. Serologic evidence is therefore correspondingly more important.

In support of the opinion that a positive Wassermann reaction in the pregnant woman means syphilis almost as surely as in the nonpregnant woman, the serologic tests at the Chicago Lying-In Hospital have been summarized for the period since the adoption of the Kolmer technic. This modification of the original Wassermann technic has given cleancut results and steadiness of strength combined, I believe, with sensitiveness and great reliability. With it I have used my glycerinized positive control,[6] a titration of pooled positive serums preserved by glycerine, and fluctuation in the strength of the reaction has seldom been greater than one point up or down.

In 7,768 pregnant women, 580 had from one to seven positive Wassermann reactions, 7.5 per cent of the whole number. These patients are separable into four groups.

1. Those attending the clinic at the hospital, a group containing few Mexicans and negroes—2,694 cases in which there were 3.1 per cent positive Wassermann reactions.

2. Those attending the Maxwell Street dispensary, a group containing an appreciable number of Mexicans and negroes—2,878 cases in which there were 8.3 per cent positive reactions.

3. Those attending the stock yards dispensary, a group similar to group 2—1,382 cases in which there were 7.4 per cent positive reactions.

4. The Provident Hospital group of 814 negroes, in which there were 19.2 per cent positive reactions.

Because of lack of data, it was impossible to summarize the fourth group. The other three totaled 6,950 cases, in which there were 424 positive reactions, or 6 per cent. This corresponds exactly with a summary of the three small groups tested in the period before the Kolmer technic was used, which contained only 277 cases.[7] These were likewise separable into groups ranging in the number of positive reactions from 3.6 in the private patients to nearly 10 per cent in charity patients.

Of the patients who gave positive reactions in the present series, 123 had two or more tests. This repetition, which is attempted in

5. Solomon, H. C.: Pregnancies as a Factor in the Prevention of Neurosyphilis, Am. J. Syph. **10**:96 (Jan.) 1926.

6. Stillians, A. W.: A Proposed Standardization of the Wassermann Reaction, Am. J. Syph. **1**:767, 1917.

7. Cornell, E. L., and Stillians, A. W.: The Value of the Wassermann Reaction in Pregnancy, J. A. M. A. **72**:551 (Feb.) 1919; Syphilis in Pregnancy and Labor, Am. J. Syph. **4**:342, 1920.

every patient suspected of having syphilis, was confirmatory in 117. Of the other six, in which the second test was negative, one bore a syphilitic child, two had two positive flocculation tests each, while in the other three, confirmatory evidence was not discovered. In my opinion, this occurred only because of lack of evidence, but there is a possibility of false positive reactions. Though it may be argued that the flocculation tests are not yet sufficiently well known to be used to establish a diagnosis of syphilis, it is unlikely that a false positive Wassermann reaction and two false positive flocculation tests would occur in the serum of the same patient. Three single positive Wassermann reactions unsupported by other tests are thus left as possible false reactions, 2.5 per cent of the positive reactions or 0.15 per cent of the whole series, one in 750.

In seven other patients who had only one serologic examination, the disease was confirmed by unmistakable evidence of syphilis in the stillborn infant, either by roentgen-ray examination or by section. The diagnosis in six others with a single serum test was supported by clinical evidence of syphilis in mother or child or by serologic evidence in husband or children.

That such confirmatory evidence was found in so few patients who had a single serologic examination is not a measure of the amount of such evidence obtained, as by far the greater part of it pertained to those already listed as having two or more tests. It is significant, rather, of the large number of those who evaded or refused outright further examination.

The Wassermann reaction in patients having undoubted syphilis often becomes negative for a time after childbirth. This phenomenon, first reported by Menten, undoubtedly is responsible for much of the confusion regarding the serology of pregnancy. In my lists of fifty-two tests made post partum in patients whose serum had been positive during pregnancy, forty-one were also positive after parturition and eleven were negative. Of the latter, the diagnosis of syphilis was confirmed in seven by active lesions in mother or child, by persistent positive serum tests in the child, positive tests in the husband or other children, or by persistent positive tests in the mother between pregnancies; of the other four cases, three are already on the list as confirmed by multiple positive tests during pregnancy, and the fourth showed a positive test in the period before the Kolmer technic was used. Thus, doubt was not cast on the diagnosis by the Menten phenomenon in any case in this series. The flocculation tests did not show any such tendency to become negative post partum, just as they may remain positive long after the Wassermann reaction is made negative by treatment.

This brings up the question of the number of patients with latent syphilis who give negative Wassermann reactions. I have no doubt that they are numerous among pregnant women, though they are of less

importance because of their comparatively infrequent, but by no means wholly innocuous, infectiousness. Schumann and Barnes [8] reported six cases in which women with negative Wassermann reactions and no history or signs of syphilis bore children whose Wassermann reaction was strongly positive. Commiskey [9] reported the cases of eleven women with negative reactions whose infants gave positive or doubtful serologic reactions. The flocculation test should be of value in detecting some of these cases. At the Chicago Lying-In Hospital, three series of flocculation tests have been made. In a series of 380 cases, the McGlumphy test agreed with the Wassermann reaction in 92.6 per cent. In 1,671 cases, the Kahn method agreed with the Wassermann method in 95.16 per cent. The Meinicke test agreed with the Wassermann test in 94.9 per cent of 1,058 cases. These results correspond closely with reports of similar comparative series from many other sources. It is true that false positive Wassermann reactions occur frequently in the serum of pregnant women, it must also be true that false positive flocculation tests have the same frequency and occur in the same cases. It is much easier for me to explain this parallelism by conceding that both are caused by syphilis.

SUMMARY

1. In a series of 6,954 pregnant women, mostly white, 6 per cent had positive Wassermann reactions.

2. In a series of 814 pregnant negroes, 19.2 per cent had positive Wassermann reactions.

3. The false positive Wassermann reaction occurred in not more than 2.5 per cent of the positive cases in this series; in all probability, much less frequently.

4. False negative reactions, both complement-binding and flocculation, often occur in pregnancy.

5. The flocculation tests are valuable aids in the diagnosis of syphilis in pregnancy.

6. The Wassermann reaction has almost the same diagnostic value in the pregnant as in the nonpregnant woman.

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8. Schumann, E. A., and Barnes, C. S.: Syphilis and Childbirth, Am. J. Obst. & Gynec. **2**:612, 1921.

9. Commiskey, L. J. J.: Routine Wassermann Reactions in Hospital Obstetrics, Am. J. Obst. **73**:676, 1916.

THE EFFECT OF EXTREMELY HOT BATHS IN EXPERIMENTAL SYPHILIS

FURTHER STUDIES *

JAY FRANK SCHAMBERG, M.D.
AND
ANNA RULE
PHILADELPHIA

In a communication entitled "Studies of the Therapeutic Effect of Fever in Experimental Rabbit Syphilis," [1] we stated that rabbits could be protected from syphilis after intratesticular inoculation of spirochetes, if they received eleven consecutive daily hot baths under certain conditions. The average rise of temperature induced in the rabbits was 4 F.

We also asserted that we had found that if a spirochetic suspension were heated on a water bath in a test tube for one hour at 41 C. (106 F.) it was incapable, as a rule, of producing syphilis, although under the darkfield microscope the spirochetes were numerous and motile.

It is proper for us to say that a repetition of this experiment did not terminate in quite the same manner. In January, 1927, we inoculated eighteen rabbits with syphilis. Six were inoculated with a spirochetic suspension which had been heated on a water bath for one and one-half hours at 40 C.; the remaining twelve were inoculated with unheated spirochetes. The latter all developed a syphiloma of the testicle with numerous spirochetes present, between the twentieth and the thirty fourth day after inoculation.

At this time all of the rabbits inoculated with heated spirochetes did not show any evidence of the disease. On the fifty-sixth day, however, one rabbit gave a positive reaction. One rabbit showed a syphiloma of the testicle on the fifty-ninth day, one on the eightieth and two on the eighty-eighth day after inoculation.

While these results are not in accord with our previously published observation, they indicate that the heating had attenuated the virulence of the spirochetes to such a degree that several of the rabbits did not manifest evidences of syphilis for nearly three months.

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* From the Research Institute of Cutaneous Diseases.

* Read at the Fiftieth Annual Meeting of the American Dermatological Association, May, 1927.

1. Schamberg, J. F., and Rule, A. M.: Studies of the Therapeutic Effect of Fever in Experimental Rabbit Syphilis, Arch. Dermat. & Syph. **14**:243 (Sept.) 1926.

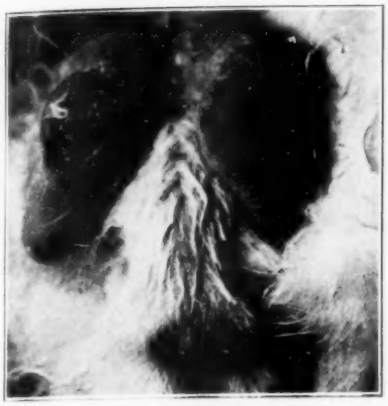

Figure 1

Figure 2

Fig. 1.—Double testicular growth. Well developed chancres of scrotum in rabbit thirty-three days after inoculation.

Fig. 2.—Appearance eighteen days after figure 1. Rabbit given fifteen hot baths; chancres healed in fourteen days.

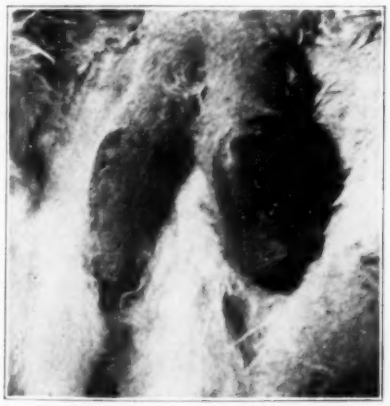

Figure 3

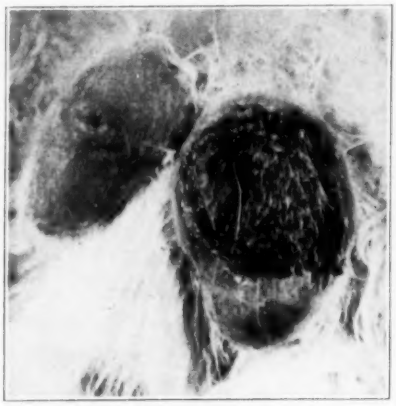

Figure 4

Fig. 3.—Well marked chancre of scrotum in rabbit thirty-three days after inoculation; untreated control.

Fig. 4.—Untreated control (same as fig. 3); photographed eighteen days later.

It is possible that the spirochetes require a maintenance of this temperature for a little longer period, and such an experiment is under way at the present time.[2]

TREATMENT IN PRIMARY SYPHILIS IN RABBITS

In a second publication on "The Therapeutic Effect of Hot Baths in Experimental Primary Syphilis in Rabbits," [3] we proved that in rabbits in which well developed chancres of the scrotum had been produced the same could be made to disappear promptly after fifteen hot baths in the course of seventeen days—indeed, almost as quickly as if arsphenamine had been injected, and more quickly than after injections of bismuth.

TABLE 1.—*Results of Experiments in Rabbits*

		Rabbits Inoculated with Suspension of Spirochetes (Unheated)		
		Feb. 17	Feb. 22	March 1
Inoculated Jan. 28	(1)	+	.....	.....
	(2)	+	.....	.....
	(3)	?	+	.....
	(4)	?	+	.....
	(5)	Neg.	?	+
	(6)	Died	.....	.....
	(7)	+	.....	.....
	(8)	Neg.	+	.....
	(9)	Neg.	?	+
	(10)	+	.....	.....
	(11)	+	.....	.....
	(12)	Neg.	+	.....

		Rabbits Inoculated with Suspension of Spirochetes, Heated for 1½ Hours at 40 C.						
		Feb. 17	Feb. 22	March 1	March 22	March 25	April 5	April 13
Inoculated Jan. 28	(13)	Neg.	Neg.	Neg.	+	.....	.....	.....
	(14)	Neg.	Neg.	Neg.	?	+	.....	.....
	(15)	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	+
	(16)	Neg.	Neg.	Neg.	Neg.	Neg.	+	.....
	(17)	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	+
	(18)	Neg.	Neg.	Neg.	Neg.	Accidental death		
		20 days	25 days	34 days	56 days	59 days	80 days	88 days

The spirochetes disappeared in less than eight days and the testicles were entirely normal in seventeen days. Spirochetes were present forty-eight hours after the first hot bath. An examination was not made for six days, when they were found absent. The exact date of their disappearance can therefore not be stated.

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2. In carrying out this experiment, it is necessary that the physiologic salt suspension of spirochetes does not contain large particles of testicular tissue and furthermore that the fluid used to inoculate be removed by a pipette and not by pouring. If the solution is poured out it is possible that it may carry along spirochetes clinging to the wall of the test tube higher up that have not been subjected to the temperature of the water bath.

3. Schamberg, J. F., and Rule, A. M.: The Therapeutic Effect of Hot Baths in Experimental Primary Syphilis in Rabbits, J. A. M. A. **88**:1217 (April 16) 1927.

In order to determine whether the infection in the animals was extinguished, the popliteal and inguinal glands were removed on the seventy-sixth day and inoculated into the testicles of two other rabbits.

These rabbits were kept under observation for eighty-seven days, and were found entirely well at the end of this period.

Having shown that syphilis in the rabbit could be prevented by hot baths and having demonstrated that primary syphilis could be cured by this procedure, we endeavored to determine the effect of raising the body temperature on secondary lesions.

In our experience, secondary syphilitic manifestations in the rabbit are uncommon.

Fig. 5.—Appearance of secondary syphiloma on hind foot of a rabbit fifty-six days after inoculation.

TREATMENT OF SECONDARY SYPHILOMA

In order to provoke generalization of the infection, we followed the plan of Pearce and Brown, and castrated the infected testicle ten days after inoculation.

Of fifteen rabbits, only one developed a well defined secondary syphiloma, which on the fifty-sixth day after inoculation had grown to about 2 cm. in length by 1.5 cm. in width; it was situated just above the hind foot (fig. 5). Puncture of this growth yielded some serum which under the dark-field microscope was full of spirochetes.

On the fifty-sixth day, this rabbit was subjected to fifteen daily hot baths (excluding Sundays and holidays). On the sixtieth day, the lesion was much smaller and spirochetes could no longer be found. At the same time the syphiloma of the other testicle which had developed and which had shown numerous spirochetes was regressing and had become negative for spirochetes. Seven days later, or eleven days

after the institution of baths, the cutaneous lesion had disappeared. The testicle had also become normal.[4]

One hundred and thirty-eight days after the primary inoculation, the popliteal and inguinal glands were removed, suspended in salt solution and transplanted into two other rabbits.

In thirty-six days these rabbits developed syphilomas of the testicle which showed numerous spirochetes.

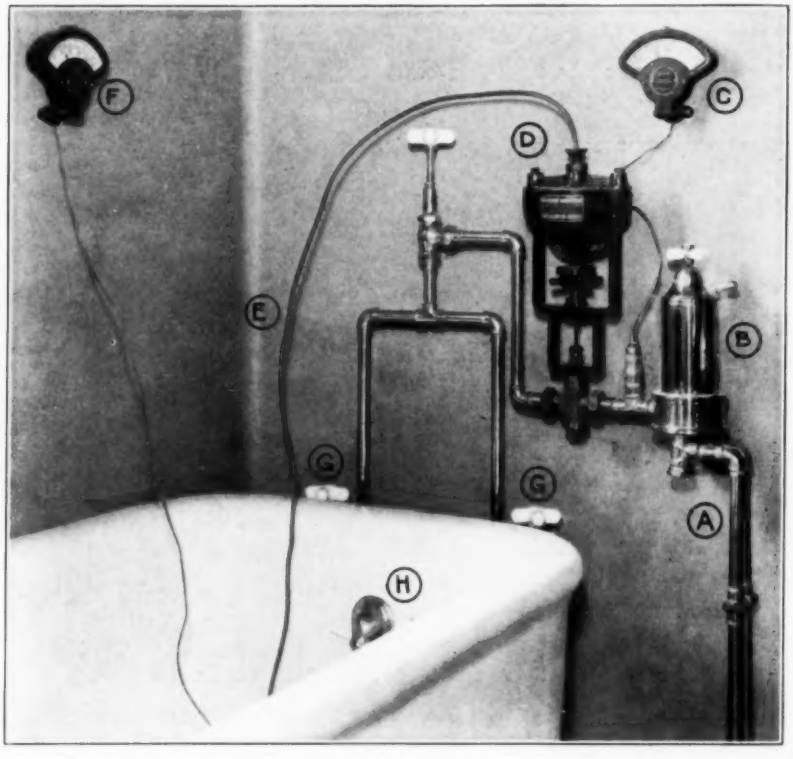

Fig. 6.—Arrangement of apparatus. *A* is the hot and cold water pipes; *B*, constant discharge temperature mixing valve; *C*, wall thermometer; *D*, control valve; *E*, capillary tube; *F*, thermometer to show temperature of tub; *G*, regular control valves; *H*, supply nozzle.

This experiment teaches, as one perhaps might have expected, that the number of hot baths required permanently to sterilize a rabbit with primary syphilis will not suffice in secondary syphilis.

DESCRIPTION OF APPARATUS

Figure 6 shows the arrangement of the apparatus.

A tub of standard make, 6 feet 6 inches long is shown.

4. The average degree of elevation of temperature was 4.1 F.

Hot and cold water enter through pipes *"A,"* passing through a constant discharge temperature mixing valve *"B."* This temperature is registered on wall thermometer *"C."*

Water then passes through control valve *"D"* which controls the amount of water passing through the valve, according to the temperature of the water in the tub. This valve is actuated by a bulb in the bottom of the tub working through capillary tube *"E."*

From valve *"D"* the water passes to the supply nozzle *"H"* which is extended and provided with a horizontal ejector type nozzle at the bottom of the tub. The purpose of this nozzle is to obtain mixing and agitation.

The regular control valves *"G"* are provided to permit manual changes if desired.

In operation, the control valve *"B"* is set for a slightly higher temperature than that desired in the tub, and the control valve *"D"* is set for the exact temperature required.

Valve *"D"* functions to admit just sufficient water to maintain the required temperature and further serves as a check should the temperature of water delivered by valve *"B"* become excessive.

Thermomter *"F"* indicates the temperature in the tub.

Wall type thermometers were used to facilitate supervision by the nurse.

With the combination of valves shown, danger of scalding is remote.

TREATMENT OF PATIENTS WITH SYPHILIS

In view of the rather astonishing effects of raising the temperature of syphilitic rabbits in the course of the disease, the query naturally suggested itself, Could this method of treatment have any practical value in the treatment of human beings with syphilis? It should be realized that syphilis in the rabbit runs a milder course than in man. It does not ordinarily lead to generalized lesions, and involvement of the central nervous system is a great rarity. On the other hand, malaria and other fever-inducing agencies are known to exert a favorable influence in certain types of syphilis, although the mechanism of the therapeutic effect is still shrouded in obscurity.

We have been trying out hot baths in the treatment of patients with syphilis, and we have found that we can effect a considerable elevation of the body temperature by this means. The temperature can be raised in some patients to 105 or 106 F., although there are individual differences in the febrile reaction.

We have devised a special bath installation for this purpose. The tub should be large enough to permit complete immersion, except, of course, of the head.

The apparatus is shown in figure 6.

TECHNIC OF BATH

The patient enters the bath water at a temperature of from 98 to 100 F. The temperature of the water is then gradually increased, so that it reaches its maximum in about 15 minutes.

An ice cap is kept applied to the head.

The highest temperature of the bath is from 110 to 114 F., which should be kept constant until the nurse or supervising physician, guided by the patient's condition, deems it wise to lower the temperature of the water. The temperature is usually maintained for from ten to fifteen minutes. It is then cooled down to 106 or 108 F. The total duration of the bath, according to the manner in which the patient tolerates it, is from thirty to fifty minutes. The patient's temperature gradually declines to normal in from thirty minutes to one hour after he leaves the bath. During this time, profuse sweating takes place. The rise and subsidence of fever are well shown in figure 7.

At the end of the bath, the patients feel quite exhausted, just as the rabbits do, but in about an hour they feel well and are able to walk about.

Dr. Seng, who consented to supervise the baths personally, has made detailed studies of their effects on temperature, respiration, pulse, blood pressure and leukocytes. These will be published in full in a forthcoming report. He has also kept accurate records and notes of the influence of the baths on the Wassermann reaction and on the clinical symptoms in the patients under treatment.

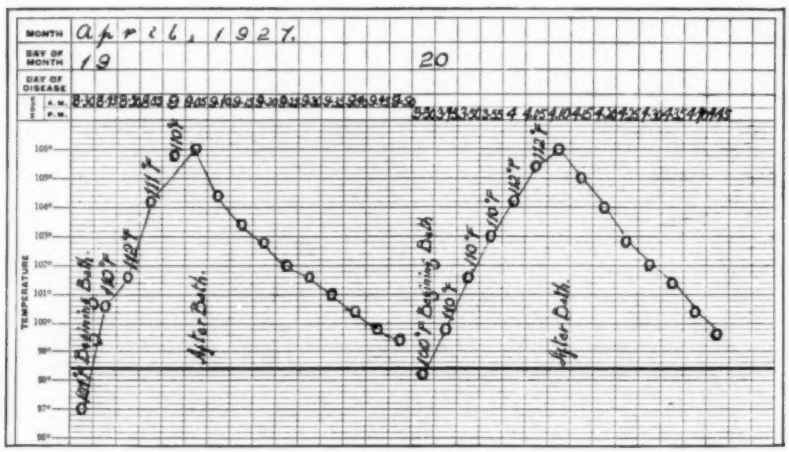

Fig. 7.—Temperature curves representing elevation of body temperature by two successive hot baths.

Mr. Brown of the Research Institute of Cutaneous Medicine has made the chemical examinations of the blood, a description of which follows.

EFFECT ON CERTAIN CHEMICAL CONSTITUENTS OF THE BLOOD

Studies of the urea nitrogen and the uric acid both before and immediately after the baths indicate that there is no material influence on the quantities of these substances in the blood. The blood cholesterol is, however, consistently reduced. On an average, there is a 10 per cent reduction. In one case, it dropped from 160 to 122 mg. This is what one would expect in view of the known observation that elevation of the body temperature lowers the blood cholesterol.

The blood sugar is increased, on an average, about 10 per cent.

Some studies on the effect of the hot baths on the enzymes of blood would indicate that the proteolytic and lipolytic power of the blood are not influenced.

CLINICAL RESULTS

We hesitate to present any report on the clinical results achieved by the baths for several reasons. The study has been purely experimental, and there was no precedent except the experiments on rabbits to guide us as to the procedure. We had no means of knowing in which types of syphilis, if in any, the response would be favorable. The period of therapeutic trial has been too short and the number of cases too small to permit of satisfactory deductions. A brief summary of the cases follows. (The data will be presented more extensively in a future publication.)

TABLE 2.—*Effects of Hot Baths on Blood*

	Cholesterol per 100 Cc. of Blood		Sugar per 100 Cc. of Blood	
	Before Bath	After Bath	Before Bath	After Bath
1. E. W.	165 mg. 148 mg.	122 mg. 120 mg.	81 mg.	80 mg.
2. G. L.	176 mg.	160 mg.	85 mg. 81 mg.	85 mg. 87 mg.
3. Z. F.	148 mg.	145 mg.	84 mg. 81 mg.	97 mg. 93 mg.
4. L. T.	155 mg.	140 mg.	68 mg. 74 mg.	74 mg. 85 mg.
5. E. J.	150 mg. 142 mg.	128 mg. 134 mg.	79 mg. 81 mg.	88 mg. 91 mg.
6. K. G.	151 mg.	150 mg.	78 mg.	75 mg.

REPORT OF CASES

CASE 1.—W. S., a colored man, aged 34, had an early tertiary serpiginous eruption. The results of the Kolmer modification of the Wassermann reaction were: ++++. ++++. ++++. ++++; the result of the Kahn test were: ++++. ++++. ++++. ++++. The patient discontinued treatment after the sixth bath. The eruption became much fainter.

After the treatment, the Wassermann reaction (Kolmer) was 4 4 3 — —; Kahn, 3 3 4.

CASE 2.—W. G., a colored man, aged 21, had a discrete annulopapular eruption on the arms and eyelids and condylomas. The results of the Kolmer modification of the Wassermann reaction were: ++++. ++++. ++++. +++, —; the results of the Kahn test were: O. ++++. ++++. The lesions on the arms disappeared after five baths.

After the treatment, the Wassermann reaction test (Kolmer) was: ++++. ++++. ++++. +++; the Kahn test was: +++; ++++. ++++.

CASE 3.—N. J., white, aged 27, had a profuse generalized maculopapular eruption. Results of the Kolmer modification of the Wassermann reaction were: ++++. ++++. ++++. ++++. ++++; the results of the Kahn test were: +++. ++++. ++++.

The eruption faded somewhat after each bath, but on the following day some new lesions appeared. After fourteen baths from October 24 to November 13, the eruption was considerably improved. After the treatment, the Wassermann reaction (Kolmer) was: ++++. ++++. ++++. —. —.; the Kahn test was: ++++. ++++. ++++.

Case 4.—W. K., a white woman, aged 25, had early extensive tertiary eruptions on the trunk and extremities, consisting of somewhat infiltrated lesions.

The results of the Kolmer modification of the Wassermann reaction were: ++++. ++++. ++++. ++++. ++++.; the results of the Kahn reaction were: ++++. ++++. ++++.

After ten baths (the highest temperature being 106.2), from December 10 to December 23, the eruption had faded, leaving brownish stains. The Wassermann reaction (Kolmer) was: ++++. ++++. ++++. +++. —; the Kahn reaction was: ++++. ++++. ++++.

Case 5.—M. B., a colored woman, aged 40, had a large ulcerative gumma on the right side of the soft palate. The results of the Kolmer modification of the Wassermann reaction were: ++++. ++++. ++++; the results of the Kahn reaction were: ++++. ++++. ++++.

The lesion was said to be improved after one bath. The patient discontinued treatment.

Case 6.—In E. U., a colored woman, aged 24, the results of the Kolmer modification of the Wassermann reaction were ++++. ++++. ++++. ++++. ++++; the results of the Kahn reaction were ++++. ++++. +++. She had latent syphilis.

After seven baths, the Wassermann reaction was: ++++. ++++. ++++; the Kahn reaction was: ++. +++. ++++.

Case 7.—G. L., a woman, aged 49, had an Argyll Robertson pupil. She had hypertension with a systolic blood pressure of 178; diastolic, 114. The blood Wassermann reaction was: ++++. ++. +. —. —. —; the results of the Kahn reaction were: —. —. —.

The Wassermann reaction with the spinal fluid was negative. The fluid showed: cells, 23.6; sugar, +; globulin, slightly increased; colloidal gold curve, 3333221000.

From March 11 to March 16, 1927, four hot baths were given.

On March 19, the blood Wassermann reaction was +++. ++. —. —. —; the Kahn, —. —. —. The spinal fluid showed: cells, 17; globulin, slightly increased; sugar, +; Wassermann reaction, +; colloidal gold curve, 2222100000. The patient then received 4 injections of 100 mg. of potassium bismuth tartrate from March 25 to April 18. At the end of this time, *the Kolmer fixation test was negative, as was the Kahn test.*

Case 8.—A W., a colored woman, aged 30, developed a maculopapular syphilid on March 1, 1927. The results of the Kolmer modification of the Wassermann reaction were: ++++. ++++. ++++. ++++. ++++; the results of the Kahn reaction were: ++++. ++++. ++++. After six hot baths, the lesions had undergone marked regression.

On April 14, the Wassermann reaction (Kolmer) was: ++++. ++++. ++++. —. —; the Kahn reaction was ++++. ++++ ++++.

Case 9.—Z. F., a white man, aged 51, had a chancre thirty years previously. Between Oct. 13, 1924, and Feb. 14, 1927, he had received thirty-six injections of bismuth and twenty-two injections of neoarsphenamine, totalling 12.6 Gm. Cardiovascular and neurologic studies gave negative results. An electrocardiogram showed premature ventricular beats. The cerebrospinal fluid showed: cells, 4; sugar, 4; globulin, no increase; Wassermann reaction, negative; colloidal gold curve, negative. The blood Wassermann reaction (Kolmer) was: ++++. +++. +. —. —; the Kahn reaction was: —. —. —.

After seven baths, a material change was not noticed in the Wasserman reaction.

CASE 10.—K. G., a colored woman, aged 24, had latent syphilis. The Kolmer modification of the Wassermann reaction was strongly positive. The Kahn reaction was ++. ++. +++. Only three baths were given, when the patient discontinued treatment.

CASE 11.—E. J., a colored woman, aged 28, had a perforation of the soft palate. The Kolmer modification of the Wassermann reaction was strongly positive; the Kahn reaction was ++. +++. ++++.

After four baths, the patient discontinued treatment. The perforation was smaller and the speech improved.

These patients were subsequently given the usual antisyphilitic treatment.

COMMENT

We have derived certain impressions from the treatment of these patients with hot baths, but they are merely tentative and may be reversed by further experience. If the quantitative Wassermann reaction by the Kolmer method is compared before and after treatment, it will be found that in nearly all instances the complement fixation test had become somewhat weaker after the treatment. In nearly all of the cases, the eruption tended to undergo regression after the treatment with baths. This was more evident with tertiary lesions than with secondary manifestations. In case 7, four injections of bismuth after four baths were followed by a negative blood Wassermann reaction in a patient who primarily had a moderately strong Wassermann reaction.

Our first endeavor was to study the effect of the hot baths alone on early and late cutaneous syphilis. We did not anticipate that this treatment of itself would suffice, but that it would have to be conjoined or followed by the usually approved methods.

Our next step will be to determine whether the associated use of very hot baths with antisyphilitic remedies will lead to shorter or surer results, both in early syphilis and in tertiary syphilis and neurosyphilis.

In connection with the use of very hot baths, it is interesting to note that the natural hot springs at Kusatsu in Japan, in which persons bathe for from three to four minutes in water of a temperature of from 113 to 125 degrees, are said to be used particularly for the "illness that destroys the nose."

CONCLUSION

In conclusion, we would emphasize the opinion that deductions cannot be drawn from the clinical results already referred to. They have been inserted to satisfy the curiosity that might be aroused by reference to a clinical trial of the method, rather than to interpret the results thereof. Conclusions can be arrived at only after a much more extended investigation.

INTRAVENOUS INJECTIONS OF BISMUTH COMPOUNDS IN THE TREATMENT OF SYPHILIS

ITS USE CLINICALLY AND IN EXPERIMENTAL SYPHILIS IN RABBITS *

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The result of clinical observations and those of experimental and microscopical research should always be considered together. It is not for good that either should be allowed to rank as a court of appeal from the decisions of the other. There are special liabilities to error which are incident to each, and when their conclusions differ, the case should be tried over again.

JONATHAN HUTCHINSON in "Syphilis" (preface, new edition).

There is an increasing tendency to administer bismuth compounds intravenously in the treatment of patients with syphilis, and an increasing number of commercial preparations of bismuth for such use are appearing. The knowledge imparted by many investigators, that bismuth compounds are considerably more toxic administered intravenously than intramuscularly, apparently has not deterred the clinical employment of the drug by this route. Since it is so employed, it becomes desirable that its status in experimental syphilis in rabbits be defined. Accordingly, this study was conducted for the purpose of determining the toxicity of different compounds of bismuth administered intravenously into rabbits and the therapeutic indexes; of comparing such indexes with those of other spirocheticidal drugs; of correlating toxicity and therapeutic activity with the percentage of the metal bismuth contained in different bismuth compounds, and of studying the therapeutic activity of bismuth compounds injected intravenously in the treatment of patients suffering with acute syphilis.

Pioneer investigations with the intramuscular administration of the drug have been conducted by Sazerac and Levaditi [1] in 1922, and subsequent investigations, by Plaut and Mulzer,[2] Hopkins,[3] Klauder [4]

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* Read at the Fiftieth Annual Meeting of the American Dermatological Association, Baltimore, May, 1927.

* From the Research Institute of Cutaneous Medicine.

1. Sazerac, R., and Levaditi, C.: Étude de l'action thérapeutique du bismuth sur la syphilis, Ann. de l'inst. Pasteur **36**:1, 1922. Levaditi: Le bismuth dans la traitement de la syphilis, Paris, Masson & Cie, 1924.

2. Plaut, F., and Mulzer, P.: Ueber die Wirkung neuer Wismutpräparate bei der experimentellen Kaninchensyphilis, München. med. Wchnschr. **70**:487, 1923.

3. Hopkins, J. G.: Bismuth in Treatment of Syphilis, Arch. Dermat. & Syph. **7**:745 (June) 1923.

4. Klauder, J. V.: Bismuth in the Treatment of Syphilis: Report of Clinical and Experimental Studies, Arch. Dermat. & Syph. **7**:721 (June) 1923.

and others. Fewer studies have been reported for the purpose of determining the therapeutic index (ratio between the maximum tolerated and therapeutically active dose) of bismuth compounds administered intravenously in experimental syphilis in rabbits.

Giemsa [5] and also Sei [6] studied the effect of intravenous injection of one bismuth compound—sodium bismutyltartrate—in experimental syphilis in rabbits. Kolle,[7] in an elaborate report, studied the effect of many different compounds administered intravenously and intramuscularly in syphilitic rabbits. The results of such studies are similar to the results of the study herein reported, and are later discussed.

It is interesting to note, that in 1919, when Kolle and Ritz [8] studied colloidal bismuth compounds given intravenously to rabbits with syphilis, they found the therapeutic index so low that further studies with bismuth compounds were abandoned.

EXPERIMENTAL STUDIES

The following preparations of bismuth compounds were employed and were injected intravenously into rabbits: Potassium bismuth tartrate, sodium bismuth tartrate, sodium bismuth gallate,[9] colloidal bismuth hydroxide, colloidal bismuth phosphate and colloidal bismuth.

Spirocheticidal Action.—In studying the spirocheticidal activity of various drugs, including bismuth compounds, in experimental syphilis in rabbits, different investigators speak of the therapeutic active dose of the drug studied as that which caused an involution of the syphiloma in the testes of rabbits in a variable number of days, from six to fourteen, and even longer, after the administration of the drug. Likewise, the rate of disappearance of *Spirochaeta pallida* is variably mentioned as occurring in from one to three or four days, or longer, after the administration of the drug. Again, some investigators mention only the curative dose without defining its meaning. There is doubt whether this dose refers to the cure of the syphiloma or the cure of the infection. The therapeutic index would of course be different in either event. There

5. Giemsa, G.: Die Chemotherapie der syphilis durch Wismutverbindungen, München. med. Wchnschr. **69**:1452, 1922.

6. Sei, S.: Experimentelle Studies mit Natrium tribismutyltartarat, Deutsche med. Wchnschr. **49**:1327, 1923.

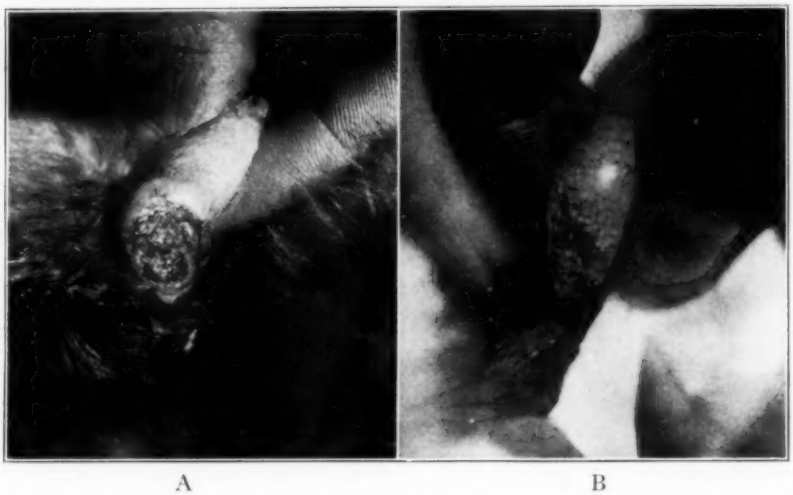
7. Kolle, W.: Chemotherapeutische Studien über Wismut, Med. Klin. **20**: 1096, 1924.

8. Kolle, W., and Ritz, H.: Experimentelle Untersuchungen über die Kaninchensyphilis mit besonderer Berücksichtigung des Silbersalvarsans, Deutsche med. Wchnschr. **49**:481, 1919.

9. Studies of the Spirocheticidal Activity of this Drug Have Been Made by Raiziss and Sazerac: Curative Effect of Bismuth Compounds in Experimental Rabbit Syphilis, Arch. Dermat & Syph. **12**:661 (Nov.) 1925, and the drug was obtained from them.

is therefore a discrepancy in the figures of the different writers relative to the therapeutic active dose and the therapeutic index of spirocheticidal drugs. The discrepancy intimately concerns the criterion employed in the evalution of this dose. Differences in the size of the syphiloma of the rabbit which has been treated is a factor in determining the rate of its disappearance after the administration of a given amount of spirocheticidal drug.

The criterion adopted in determining the therapeutically active dose of the preparations studied is that employed in previous studies.[10] Rabbits that had syphilomas of approximately the same size were utilized. The results following the administration of the therapeutically active dose of arsphenamine, that is, 0.006 Gm. per kilogram of body weight injected intravenously into rabbits with active syphilitic testicular



A B

Fig. 1.—Experimental scrotal chancre in rabbit; *A*, before treatment with 0.006 Gm. per kilogram of body weight of arsphenamine injected intravenously; *B*, after treatment.

lesions, are taken as a standard. (The curative dose of arsphenamine is about 0.012 Gm. per body weight, injected intravenously.) Figure 1 shows the gross result. Before treatment, the dark-field examination of the surface of the chancre, or, in its absence, of serum obtained from puncturing the testicular nodes, showed many motile spirochetes in each microscopic field. Twenty-four hours after treatment, the dark-field examination showed only a few slightly motile or nonmotile spirochetes and many agglutinated organisms in each field. Results of dark-field

10. Klauder (footnote 4); Comparative Spirocheticidal Activity of Salts of Metals not Heretofore Studied in the Treatment of Experimental Rabbit Syphilis, Arch. Dermat. & Syph. **9**:219 (Feb.) 1924.

examinations on subsequent days were negative. Grossly, the chancre or the nodes were appreciably smaller the following twenty-four hours, and they gradually lessened in size until complete involution occurred within eight days. The testicular or scrotal syphilitic lesions did not recur during the following two months. In some animals, active syphilitic lesions recur after this period.

TABLE 1.—*Comparative Spirocheticidal Activity of Different Compounds of Bismuth Administered Intravenously in Experimental Syphilis in Rabbits*

		Testicle of Rabbit with Syphiloma		
Drug	Grams per Kilogram	24 Hours After Treatment	8 Days After Treatment	Comment
Potassium bismuth tartrate	0.002	No gross change; dark field, nonmotile spirochetes	Involution not complete, chancre crusted area, small node in testes	Involution complete in sixteen days; recurrence, six weeks
	0.003	Gross change; dark field, few nonmotile	Involution complete	
	0.004	Gross change; dark field, few nonmotile	Involution complete	
Sodium bismuth tartrate	0.003	No gross change; dark field, nonmotile	Marked change; involution not complete	Involution complete in ten days
	0.004	Gross change; dark field, few nonmotile	Died on fifth day, involution not complete at death	
Sodium bismuth gallate	0.003	Gross change; dark field, few nonmotile	Marked change, involution not complete	Involution complete in ten days
	0.005	Gross change; dark field, few nonmotile	Involution complete	Died on eighth day
Colloidal bismuth hydroxide	0.004	Gross change; dark field, few nonmotile	Small node present	Involution complete in fourteen days
	0.005	Gross change; dark field, few nonmotile	Involution complete	No recurrence; four months observation
	0.006	Marked gross change; dark field, few nonmotile	Involution complete	No recurrence; six months observation
Colloidal bismuth phosphate (high dispersive state)	0.003	Gross change; dark field, few nonmotile	Involution complete	
Colloidal bismuth phosphate (low dispersive state)	0.003	Gross change; dark field, few nonmotile	Involution complete	
Colloidal bismuth	0.005	No gross change; dark field, many nonmotile	Dead, involution not complete; nodes present	Died sixth day
	0.006	No gross change; dark field, many nonmotile	Dead, involution not complete; nodes present	Died sixth day

Table 1 is a protocol of the studies to determine the therapeutically active dose of the different preparations of bismuth compounds. The therapeutically active dose of these preparations is shown in table 2, also their bismuth content and the therapeutically active dose expressed in terms of the metal bismuth. In order to insure accurracy, in so far as the percentage of bismuth in the compounds studied is concerned, quantita-

tive determination of bismuth compounds were conducted. The figures thus obtained were utilized in the compilation of table 2. It will be seen that the therapeutically active dose of the compounds varied, from about 0.003 Gm. per kilogram of body weight to about 0.005 Gm. This variation did not exactly correspond to the percentage of bismuth contained in the compounds. Expressed in terms of the metal bismuth, the therapeutically active dose varied from 0.0026 Gm. per kilogram of body weight to about 0.004 Gm.

It will also be seen in table 2 that the therapeutically active dose was close to the maximum tolerated dose with some preparations and exceeded this dose with others; for example, 0.005 Gm. per kilogram of sodium bismuth gallate caused involution of the syphiloma within eight days in accordance with the standard employed, but this dose killed the

TABLE 2.—*Showing Therapeutic Index of Different Compounds of Bismuth Administered Intravenously in Experimental Syphilis in Rabbits*

Drug	Bismuth Content, per Cent	Therapeutically Active Dose of Compound, Gm. per Kg.	Therapeutically Active Dose of Metal Bismuth, Gm. per Kg.	Maximum Tolerated Dose of Compound, Gm. per Kg.	Maximum Tolerated Dose of Metal Bismuth, Gm. per Kg.	Therapeutic Index
Potassium bismuth tartrate.....	65	0.003	0.0026	0.005	0.0033	One and two-thirds
Sodium bismuth tartrate.....	68	0.003+	0.002+	0.003	0.002	Less than one
Sodium bismuth gallate.....	63	0.005	0.0031	0.003	0.0019	Less than one
Colloidal bismuth hydroxide.....	80	0.0048	0.0038	0.0086	0.0069	One and eight-tenths
Colloidal bismuth phosphate*.....	68	0.003	0.002	0.025	0.017	Eight and one-third
Colloidal bismuth.....	..	0.004+	0.004+	0.004	0.004	Less than one

* This preparation is in all probability bismuth acid phosphate. The computation of the percentage of bismuth is based on this assumption.

rabbit in eight days. The maximum tolerated dose of 0.003 Gm. did not cause involution within the limits of the standard.

In all the preparations, the bismuth radical was loosely bound, except in sodium bismuth gallate, which occupies a position midway between the compounds in which the bismuth radical is loosely bound and those in which it is firmly bound. It was hoped to correlate the therapeutic activity and toxicity with the position of the bismuth radical. Firmly bound bismuth compounds are not available, and are extremely difficult to prepare. It may be recalled that the spirocheticidal activity and toxicity of mercurial preparations correspond to the chemical structure. Compounds in which the mercury radical is loosely bound are more spirocheticidal and at the same time more toxic, and vice versa.

TOXICITY OF BISMUTH ADMINISTERED INTRAVENOUSLY

Although rabbits tolerate bismuth compounds poorly, these animals were employed since the therapeutic index could not be determined in any other animal.

Many investigators have shown that the rat tolerates about four times as much bismuth compounds per kilogram, administered intravenously, as the rabbit, and about three times as much when the drug is injected intramuscularly. Moreover, there is an unusual variation in the tolerance of rabbits to bismuth; indeed, Pomaret [11] observed that white rabbits tolerated more than dark rabbits. According to Didry,[12] the toxic dose of bismuth compounds administered intravenously to dogs is 0.04 Gm. of the metal bismuth per kilogram. The varying tolerance of rabbits to bismuth compounds should be borne in mind in the consideration of the reported results of experimental studies by different investigators.

It will be seen in table 2 that the maximum tolerated dose of the bismuth compounds studied varied from 0.003 Gm. per kilogram to 0.025 Gm. Expressed in terms of the metal bismuth, it varied from 0.002 Gm. per kilogram to 0.017 Gm. Comparable to the therapeutically active dose, the maximum tolerated dose did not correspond to the amount of the metal bismuth injected. It is interesting to note that colloidal bismuth phosphate was the least toxic of the preparations studied. The maximum tolerated dose of this drug was 0.025 Gm. The next less toxic preparation was colloidal bismuth hydroxide, with a maximum tolerated dose of 0.0086 Gm. This lessened toxicity can perhaps be attributed to the colloidal state, yet the therapeutically active dose of these drugs was not correspondingly greater.

Colloidal bismuth was relatively toxic. The maximum tolerated dose was 0.004 per kilogram of the compound, which was all metallic bismuth. The therapeutic index was less than 1. It should be stated that at the time the preparation was obtained and injected, the metal bismuth was no longer in a colloidal suspension but had precipitated. As previously stated, Kolle and Ritz [8] obtained a low therapeutic index with colloidal bismuth. Lacapère and Galliot [13] observed that rabbits injected with more than 0.005 Gm. per kilogram of colloidal bismuth did not survive.

It is well known that lethal doses of bismuth produce a severe nephritis in animals, which is apparently the cause of death. A detailed study of this toxicologic reaction in rabbits has recently been reported by Lucke and Klauder.[14]

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11. Pomaret, in discussion on Lacapère and Galliot: Bull. Soc. franç. de dermat. et syph., 1922, no. 5, p. 215.

12. Didry, in discussion on Lacapère and Galliot: Bull. Soc. franç. de dermat. et syph., 1922, no. 5, p. 210.

13. Lacapère and Galliot: Presentation d'un composé bismuthique injectable dans les veines. Prémiérs resultats, Bull. Soc. franç. de dermat. et syph, 1922, no. 5, p. 210.

14. Lucke, Baldwin; and Klauder, J. V.: Histological Changes Produced Experimentally in Rabbits by Bismuth, J. Pharm. & Exper. Therap. **21**:5, 1923.

Sometimes when large doses of bismuth compounds are injected intravenously into rabbits, the animals die suddenly, apparently from an involvement of the respiratory center. Orfila [15] and, more recently, Didry [12] and others have shown that acute poisoning with bismuth compounds is manifested by a primary stage of motor excitement, followed shortly by paralysis of the respiration and cardiac action. As will be discussed later, these symptoms have been observed in sudden deaths following the clinical use of bismuth compounds intravenously.

Spirocheticidal Activity, Toxicity in Relation to Bismuth Content.—It is interesting to note that of the many compounds of bismuth studied by Kolle,[7] the toxicity and therapeutic activity varied considerably. Some were much less toxic than others with the same or even greater therapeutic activity. Mention could be made in this regard of mannose sodium bismuthate, mannose sodium nitrate, bismuth subnitrate and sodium bismuth iodoquininsulphate. The maximum tolerated dose of these preparations varied from 0.01 Gm. to 0.03 Gm. per kilogram, injected intravenously into rabbits, and the therapeutic index varied from 3.3 to 4. Moreover, from Kolle's [7] figures, the therapeutic index could not be correlated with the bismuth content, for example, mannose-sodium bismuthate with a bismuth content of 19 per cent and a therapeutic index of 4 with this drug although the bismuth was low, the therapeutic index was high. In the foregoing regard, the results obtained in this study corroborated Kolle's observations. It is to be noted that the bismuth compounds preparations studied were different from those studied by Kolle. Mention could also be made of the drug studied by Grenet, Drouin and Richon,[16] a sodium derivative of trioxybismuthobenzoic acid, with a 50 per cent bismuth content, which was tolerated intravenously in rabbits in a dosage of 0.01 Gm. per kilogram. In their report, however, mention was not made of its therapeutic activity.

It appears, therefore, from observations herein reported and from the foregoing observations of others, that there is a varying toxicity, therapeutic activity and therapeutic index of bismuth compounds administered intravenously [17] into rabbits, and such variation does not exactly correspond with the bismuth content of the compound. It has perhaps been generally recognized that the therapeutic activity of bismuth

15. Orfila: Bismuth, in Richet, C.: Dictionnaire de physiologie, Paris, F. Alcan, 1895, vol. 2, p. 219.

16. Grenet, H.; Drouin, H., and Richon, L.: An Aromatic Bismuth Compound in the Treatment of Syphilis, Bull. Acad. de méd., Paris **87**:658, 1922.

17. The therapeutic activity of bismuth compounds in experiments on rabbits is perhaps more accurately studied by intravenous administration than by intramuscular administration, since the rate of absorption of the drug following intramuscular injection is a complicating factor.

compounds is more intimately concerned with their bismuth content than has been substantiated in experimental studies.

In view of the foregoing observations, there is a possibility in the domain of chemotherapy of the preparation of a bismuth compound with a higher therapeutic index than has yet been obtained; herein rests the future of the use of intravenous administration of bismuth in the treatment of patients with syphilis.

THERAPEUTIC INDEX OF BISMUTH ADMINISTERED INTRAVENOUSLY IN COMPARISON WITH OTHER SPIROCHETICIDAL DRUGS

Table 3 shows the therapeutically active dose, the maximum tolerated dose and the therapeutic index of arsphenamine, mercury, bismuth and

TABLE 3.—*Comparative Spirocheticidal Activity of Arsphenamine, Mercury, Bismuth and Antimony in Experimental Syphilis*

Drug	Method of Injection	Therapeutically Active Dose, Gm. per Kg.	Maximum Tolerated Dose, Gm.	Therapeutic Index
Mercuric chloride	Intravenous	0.003	0.001	One-third
Arsphenamine	Intravenous	0.006	0.100	Seventeen
Sodium and potassium tartro-bismuthate (aqueous solution)	Intramuscular	0.050	0.125	Two and one-half
Sodium and potassium tartro-bismuthate (oil suspension)	Intramuscular	0.050	0.2	Four
Potassium tartro-bismuthate	Intramuscular	0.050	0.250	Five
Bismuth trioxide (oil suspension)	Intramuscular	0.150	0.400	Two and two-thirds
Potassium bismuth tartrate	Intravenous	0.003	0.005	One and two-thirds
Sodium bismuth tartrate	Intravenous	0.003+	0.003	Less than one
Sodium bismuth gallate	Intravenous	0.005	0.0031	Less than one
Colloidal bismuth hydroxide	Intravenous	0.0048	0.0086	One and eight tenths
Colloidal bismuth phosphate	Intravenous	0.003	0.025	Eight and one-third
Colloidal bismuth	Intravenous	0.004	0.004	Less than one
Potassium antimonyl tartrate	Intravenous	.....	0.010*	Less than one
Antimony tartrate	Intravenous	.....	0.015*	Less than one
Antimony tartrate	Intramuscular	0.050	0.050	One

* With these amounts, there was little evidence of spirocheticidal activity.

antimony as determined in experimental syphilis in rabbits. It will be seen that the index of the preparations of bismuth compounds studied and administered intravenously varied from less than 1 to about 2, except in the case of colloidal bismuth phosphate, in which the index was 8.3. Of the bismuth preparations studied and administered intramuscularly, the index varied from 2.5 to 5. For comparison it will be seen that the therapeutic index of mercury administered intravenously is 0.33, less than 1 for antimony and 17 for arsphenamine.

INTRAVENOUS INJECTION OF BISMUTH COMPOUNDS IN THE TREATMENT OF SYPHILIS: REVIEW OF LITERATURE

Intravenous injection of bismuth compounds was first employed clinically as early as 1922 by Grenet, Drouin and Richon [16] and by Lacapère and Galliot.[13] Grenet, Drouin and Richon injected sodium tri-oxybismuthobenzoic acid every two days for a total of from ten

to fifteen injections, which constituted one series. The single dose corresponded to 0.03 Gm. of the metal bismuth and the total to from 0.3 to 0.45 Gm. for the series. A single injection of 0.075 Gm. of the metal bismuth was administered to some patients. The drug was well tolerated. Chancres healed in less than eight days; cutaneous lesions of secondary syphilis after four or five injections in from eight to ten days, and those of tertiary syphilis in about ten days. Spirochetes disappeared from mucous patches after the first injection. The Wassermann reaction in primary syphilis became negative after the first series of injections; it was less positive in secondary syphilis after the first series and generally negative after the second series. So far as the disappearance of spirochetes and the involution of syphilitic lesions were concerned, they concluded that the results were as favorable as those obtained with the organic arsenicals.

Lacapère and Galliot administered colloidal bismuth intravenously in doses of 0.033 Gm. of the metal, three times a week, for a total of from twenty to twenty-five injections, administered in the course of about six weeks, which totaled about 0.6 Gm. of the metal. The disappearance of spirochetes and the involution of syphilids following this treatment were similar to the results reported by Grenet, Drouin and Richon.[16] The Wassermann reaction was attenuated, and in some cases became negative after the first course of treatment.

Since these original reports were made on the intravenous administration of bismuth compounds in the therapy of syphilis, a number of other reports by foreign writers have appeared. Particular mention may be made of the following: Neuendorff,[18] Bruck and Weinberg,[19] Gutmann,[20] Engelhardt,[21] Portmann,[22] Dyboski,[23] Alker and Waldmann[24] and Mras.[25] The results obtained may be summarized as follows:

Dosage.—The dosage employed varied from 0.02 Gm. to 0.1 Gm. of the metal, administered two or three times a week, for a total of

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18. Neuendorff, quoted from Heymann, K.: Die Wismutbehandlung der Syphilis, Berlin, Hans Pusch, 1925 p. 21.

19. Bruck, C., and Weinberg, H.: Dermat. Ztschr. **39**:257, 1923.

20. Gutmann, C.: Die Intravenous Wismuttherapie Mit Nadison-Kolle, Dermat. Wchnschr. **78**:73, 1924.

21. Engelhardt, W.: Wismuttherapie der Syphilis mit einzeitig intravenos-intramusk Injectionen von Wismutsalzen, Med. Klin. **2**:570, 1924.

22. Portmann, F. W.: Erfahrungen Mit Wismut-Diasporal, Dermat. Wchnschr. **81**:1781, 1925.

23. Dyboski, T.: Ueber intravenose Einspritzungen von Calomel und Wismut-Diasporal, Dermat. Ztschr. **41**:33, 1924.

24. Alker, A., and Waldmann, E.: Ueber intravenose Wismutbehandlung der Syphilis, Deutsche med. Wchnschr. **44**:1510, 1924.

25. Mras, F.: Zur Klinik der intravenosen Wismutbehandlungen, Wien. klin. Wchnschr. **29**:724, 1924.

0.3 Gm. to about 1 Gm. of the metal. It appears from these reports that 0.05 Gm. of the metal bismuth is the proper dose for a single injection. Gutmann administered as much as 0.125 Gm. per dose, following which he always observed toxicologic symptoms. Heymann [26] gave 0.1 Gm. per week as the proper dosage; more than this he states is dangerous, as toxic symptoms may be produced.

Clinical Results.—The spirochetes invariably disappeared from the surface of chancres and mucous patches twenty hours after a single intravenous injection. Neuendorff [18] observed their disappearance from lymph nodes after a single injection. Cutaneous lesions and lesions of the mucous membrane involuted after from two to six injections.

The Effect on the Wassermann Test.—The four plus Wassermann reaction in primary and in secondary syphilis became negative in some patients after a total administration of as little as 0.3 Gm. of the metal bismuth; in others, after an amount varying from 0.3 Gm. to about 1.5 Gm.

Untoward Reaction.—The most constant reaction observed was pain in the teeth, which appeared during the injection. Every bismuth preparation administered intravenously causes this pain, which appears to be in direct relationship with the highly dispersive state of the colloidal preparation employed. Portmann observed this reaction following the injection of a bismuth preparation in a highly dispersive state, but did not observe it after injecting another preparation containing the same amount of bismuth but in a lower dispersive state. Pain in the knees and joints following intravenous injection has also been observed, but it is much less frequent than pain in the teeth.

Another common reaction is polyuria. The occurrence of fever, chills, vomiting and diarrhea appears to be in relation to the dosage; these symptoms are more likely to develop following injections of more than 0.05 Gm. of the metal bismuth. Transitory albuminuria has been observed and is more frequent following injections of more than 0.05 Gm. of the metal bismuth.

The gingival blue line of bismuth does not develop as readily and to the same extent after intravenous injections as after intramuscular injections. Stomatitis and ulcerations of the mucous membrane have been observed, but such reactions apparently are exceptional. The infrequency of the gingival blue line and stomatitis following intravenous injections of bismuth compounds can doubtless be attributed to the rapid excretion of bismuth. Fischer [27] observed the development

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26. Heymann, K.: Die Wismutbehandlung der Syphilis, Berlin, Hans Pusch, 1925, p. 13.

27. Fischer, O.: Enteritis from Bismuth Poisoning, Dermat. Wchnschr. **82**: 268, 1926.

of severe ulcerative enteritis after a course of seven intravenous injections. No other toxicologic symptoms developed, and the patient recovered.

Gastou and Pontoizeau [28] reported the occurrence of a localized pruritic papular squamous eruption following intravenous injections of bismuth compounds.

Deaths Following Intravenous Injections of Bismuth Compounds.—Magnus [29] reported a sudden death following an intravenous injection of bismuth ammonium citrate. About a moment after the injection, the patient became unconscious, had convulsions and succumbed. Autopsy failed to explain why death occurred. The patient had been treated previously with neoarsphenamine and mercury and the same bismuth preparation had been injected intravenously. He was healthy the day of the fatal injection.

Duchateau and Verstraeten [30] reported two deaths. Both patients had general paralysis and previously had been intensively treated with arsenic, mercury and bismuth preparations. Almost immediately after receiving an intravenous injection of an aqueous solution of tartrobismuthate which corresponded to 0.072 Gm. of the metal bismuth, the patient had conclusive movements, became asphyxiated and soon died.

Another sudden death is reported by Fraenckel.[31] Autopsy failed to explain the cause of this patient's death.[32]

COMBINED INTRAVENOUS BISMUTH THERAPY; DISTRIBUTION AND ELIMINATION OF BISMUTH AFTER INTRAVENOUS INJECTION

Guttmann [33] employed a bismuth compound intravenously conjointly with arsenical therapy in the three following ways:

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28. Gastou, P., and Pontoizeau, E.: Erythrodermie consecutive au traitement bismuthique colloidal intraveineux, Bull. Soc. franç. de dermat. et syph. **8**:382, 1922.

29. Magnus: Plötzlichen Todesfall nach intravenosen Wismuteinspritzung, Klin. Wchnschr. **3**:1275, 1924.

30. Duchateau, M., and Verstraeten, P.: Les injections intraveineuses de bismuth dans la paralisie générale, J. de Neurol. et Psych. **9**:567, 1925.

31. Fraenckel, P.: Two Cases of Sudden Death Following Intravenous Bismuth Injection, Deutsche Ztschr. f. d. ges. gerichtl. Med. **5**:5, 1925. Of the two cases referred to in Fraenckel's title, one is the case reported by Magnus (footnote 29).

32. A possible explanation is the occurrence of what Widal called *crise colloidoclasique* in which there is a disturbance of the colloidal equilibrium of the blood. Such disturbance easily occurs in allergic patients. Any intravenous injection is more hazardous in such patients. It is important to know if these patients were allergic.

33. Gutmann, C.: Erfahrungen mit dem Wismutprätarat Nadison in Kombination mit Neosalvarsan bei der Behandlung der Syphilis, Dermat. Wchnschr. **77**:861 and 892, 1923.

First Method.—Small doses of neoarsphenamine administered at brief intervals were alternated with injections of a bismuth compound at brief intervals. The bismuth preparation employed was potassium tartrobismuthate with colloidal bismuth hydroxide saturated. The dose of a single injection corresponded to 0.05 Gm. of the metal.

Second Method.—Mixed injections were employed according to Linser's method. Twenty-five and 50 mg. of the metal bismuth was injected with 0.2 Gm. and 0.3 Gm. of neoarsphenamine at from three to four day intervals, for a total of ten injections, making a total of 4.35 Gm. of neoarsphenamine and 0.475 Gm. of metallic bismuth.

Third Method.—The method is the same as the second with the addition of five intramuscular injections of the bismuth compound. The total administration of metallic bismuth, both intravenously and intramuscularly, was 0.6 Gm.

Engelhardt [21] injected bismuth compounds both intravenously and intramuscularly into the same patient. He studied the excretion of the drug in the urine after a single intravenous injection, after a single intramuscular injection, and after a combined injection. The preparation employed for intravenous injection was bismuthylhydroxyquinolin sodium sulphonate (yatren A) and for intramuscular injection, bismuth iodoxyquinolin sulphonic acid (yatren B). After intravenous injection, the main quantity of the injected bismuth was excreted in twenty-four hours. From one half to two thirds of this quantity was excreted in the urine, the first two and four hours after the injection. Fractions of milligrams of metallic bismuth could, however, be found after the thirty-second day of the injection. After an intramuscular injection, the maximum excretion was reached on the ninth and tenth day; from then on, it declined. Fractions of a milligram could be obtained until the fiftieth day. After a combined intravenous and intramuscular injection, a considerable excretion of metallic bismuth was noted during the first day, which reached its maximum on the second day. A gradually decreasing excretion was obtained until the fortieth day. The double injection was employed in order to maintain a higher level of retained bismuth, thereby producing the so-called "punch" action in the sense of Felke.

Memmesheimer [34] studied the retention and excretion of metallic bismuth after intravenous administration into rabbits. The drug was found in the lungs, kidneys, heart, blood, feces, urine, colon and brain. The spleen held the largest amount of bismuth; nine times as much of the metal was retained in this organ as in the liver. The excretion of

34. Memmesheimer, A.: Ueber das Verhalten intravenös eingebrachten Wismuts in Körper und seine Ausscheidung, Ztschr. f. d. ges. exper. Med. **47**:454, 1925.

bismuth increased for twenty hours, and then decreased; traces of bismuth were excreted for as long as ten weeks. Considering the excretion in the urine and feces, Memmesheimer [34] concluded that there is a considerable and continued "depot" action of bismuth in the organs after an intravenous injection of the drug.

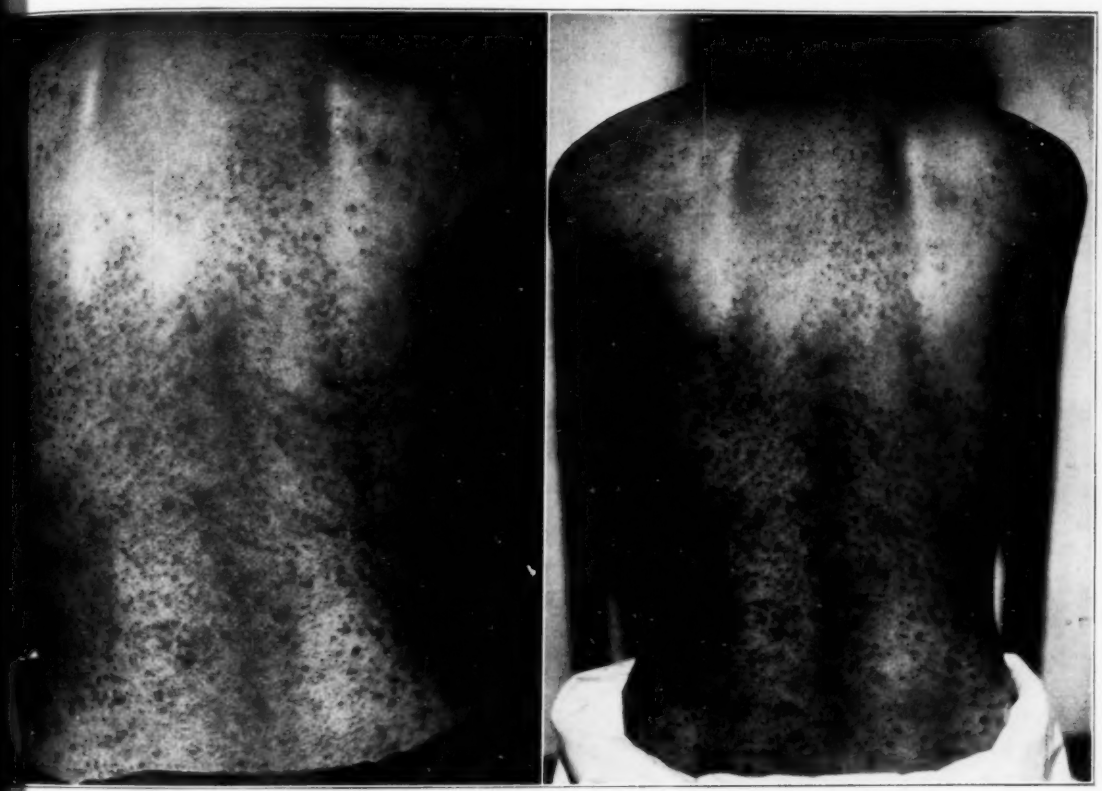
CLINICAL RESULTS OF INTRAVENOUS INJECTION OF BISMUTH COMPOUNDS

Thirty young healthy adult patients with a secondary eruption of syphilis were treated by intravenous injections of bismuth compounds. The preparation employed was colloidal bismuth hydroxide usually in doses of 0.05 Gm. diluted in 10 cc. of distilled water administered biweekly. Some of the patients were given doses ranging from 0.05 Gm. to 0.1 Gm. biweekly. Some were treated with colloidal bismuth phosphate in the advised dose of 0.025 Gm., which was administered biweekly.

Twenty-four hours after a single injection of 0.05 Gm., the spirochetes disappeared from the open surface of the syphilids. Cutaneous syphilids and syphilids of the mucous membrane involuted entirely; in some patients, the involution was unusually rapid, following as little as two injections of 0.05 Gm.; in others, with a profuse and pronounced eruption, such as large papular syphilids, as much as five or six injections were required. As far as the disappearance of the syphilids is concerned, the results of intravenous injection of bismuth compounds compared favorably with those obtained with arsenicals. The effect of intravenous injection of bismuth compounds was more pronounced than when this drug was injected intramuscularly.

Acute untoward reactions were not observed. The most frequent reaction was pain in the teeth, which appeared during the injection and usually disappeared within an hour. The pain was not sufficiently severe to cause the patient to object to the treatment. It was more likely to appear following injections of more than 0.05 Gm. and perhaps following injections of solutions of bismuth compounds in a highly dispersive state; although it was noted during the injections of 0.025 Gm. of bismuth phosphate in a highly dispersive state. One patient complained of pain in the throat when an injection was made, and another complained of pain in both knees appearing within twenty-four hours after an injection. The next most frequent reaction was polyuria, which appeared within twenty-four hours; this symptom was more frequent following larger doses than 0.05 Gm. Injections of 50 mg. were uniformly well tolerated, and most patients gained in weight; when more than this amount was used, fever, a general feeling of illness and at times chills were likely reactions. Stomatitis was not observed. The gingival black line of bismuth was observed in only one patient; he received biweekly injec-

tions of 0.1 Gm. during ten consecutive injections. Other untoward reactions did not appear, and the patient gained in weight. Albuminuria was not common. In one patient, albuminuria (light cloud) appeared after a total administration of 0.5 Gm. and led to the cessation of intravenous injections of bismuth compounds, which caused the albuminuria to disappear rapidly. At times fetor of the breath was noticed during the injection.



A B

Fig. 2.—*A* shows a well pronounced and diffuse small miliary papular eruption of syphilis of five months' duration, before the patient was treated with 0.05 Gm. of colloidal bismuth hydroxide injected intravenously. The patient also had a bilateral syphilitic iritis. *B* shows only pigmentary remains of the eruption. Involution took place after the third intravenous injection administered biweekly. The iritis also involuted.

Injections of 0.025 Gm. of colloidal bismuth phosphate were therapeutically effective. Mucous patches, as well as the less pronounced cutaneous syphilids involuted followed as little as three injections. There was no untoward reaction after injection of this drug in doses of

0.025 Gm. Considering the relatively lower toxicity of this drug in rabbits, 0.025 Gm. appears to be a conservative dosage for intravenous injection. Colloidal bismuth phosphate injected intravenously was also employed by alternating at three day intervals with colloidal bismuth hydroxide injected intramuscularly. Colloidal bismuth was also injected simultaneously intravenously and intramuscularly.

Figure 4 *A* shows a patient with a well pronounced macular eruption of three weeks' duration. He also presented a chancre of the finger. Colloidal bismuth phosphate, 0.025 Gm., was administered intravenously, and at the same time 0.2 Gm. of bismuth hydroxide was injected intramuscularly. These injections were given at three day intervals; later,

A B

Fig. 3.—At the initial treatment, this patient presented a generalized papular eruption which involuted after two intravenous injections of 0.05 Gm. of colloidal bismuth hydroxide. After another injection, the patient allowed treatment to lapse for three weeks, and then presented a papular eruption localized to face, as shown in *A*. After two intravenous injections of 0.05 Gm., the recurrent syphilid involuted, as shown in *B*.

at five day intervals, and still later, at weekly intervals. After the seventh consecutive conjoint injection, one month from the onset of treatment, the eruption and chancre were completely involuted, as is shown in figure 4 *B*. Treatment was well tolerated; untoward reactions did not occur. After the fourteenth conjoint injection, administered in the course of eleven weeks, the quantitative Wassermann reaction was completely negative. Prior to treatment, the reaction was four plus in all dilutions.

The Effect on Wassermann Reaction.—The results reported by other writers, in which the four plus Wassermann reaction of secondary syphilis frequently became negative after a total administration of 0.1 Gm. and less of the metal bismuth, was obtained only in one patient. The Wassermann reactions were performed in Dr. Kolmer's laboratory. The method employed was the Kolmer quantitative method, five dilutions of serum, ranging from 0.1 cc. to 0.0025 cc., being used. The antigen used was a cholesterolized and lecithinized alcohol extract of the muscle of the heart. At the beginning of the treatment, the reaction was invariably four plus in all dilutions. The best result obtained was a negative reaction in all dilutions after a total administration of 0.5 Gm.

A B

Fig. 4.—*A*, a well pronounced macular eruption of syphilis before conjoint injections of colloidal bismuth phosphate, 0.025 Gm., intravenously and 0.2 Gm. colloidal bismuth hydroxide intramuscularly. *B*, complete involution after the seventh conjoint injection administered in the course of one month. The Wassermann reaction became negative after the fourteenth conjoint injection administered in the course of eleven weeks.

of bismuth hydroxide injected in doses of 0.05 Gm. biweekly for ten consecutive injections. The photograph of the eruption of this patient, before and after treatment, is shown in figure 2. Albuminuria appeared in this patient after a total treatment of 0.5 Gm. Intravenous injections of bismuth compounds were discontinued. A negative reaction was not obtained in any other patient after a total treatment of 1 Gm. or less. After a total administration of 1 Gm., the reaction in all the patients

was greatly reduced; that is, it was negative in the high dilutions of serum and four plus or less in the low dilutions.

In those patients in whom treatment was continued beyond a total of 1.0 Gm., the reaction became negative after a total of about 1.5 Gm. of bismuth hydroxide, and in a few, after an amount approaching 2 Gm. In a previous study,[4] it was observed that the four plus Kolmer quantitative Wassermann reaction in secondary syphilis became negative after a total administration of from 2 Gm. to 3 Gm. or more of bismuth (tartrobismuthates and bismuth trioxide) injected intramuscularly.

After intravenous injections of 0.025 Gm. of colloidal bismuth phosphate administered conjointly with 0.2 Gm. of bismuth hydroxide intramuscularly, the Wassermann reaction became negative after not less than fourteen such injections. The total treatment required varied from about 0.3 Gm. intravenously and about 2 Gm. intramuscularly administered in the course of about three months to about 0.4 Gm. intravenously and about 3 Gm. intramuscularly administered in the course of about four months.

CLINICAL RESULTS: INTRAVENOUS VS. INTRAMUSCULAR THERAPY OF SYPHILIS

The patient whose photograph is shown in figure 3 was treated initially for a generalized papular eruption of syphilis. The eruption involuted after the second injection of 0.05 Gm. of bismuth hydroxide administered biweekly. After a similar injection, the patient allowed treatment to lapse for three weeks; at the end of this time, she presented a recurrent papular eruption localized to the face, as shown in figure 3 *A*. This recurrent syphilid involuted after two injections of 0.05 Gm. of bismuth hydroxide. It is interesting to note that apparently a bismuth-fast strain of spirochetes did not develop. The important point, however, was the brief interval between the cessation of treatment and the clinical recurrence. Another patient received biweekly injections of 0.05 Gm. of bismuth hydroxide for ten consecutive injections; then, because of irregular attendance, he received treatment at weekly and at longer intervals. Following less regular treatment, the Wassermann reaction in the higher dilutions of the quantitative method, previously negative became positive. This rapid clinical and serologic recurrence of the disease is consistent with the rapid excretion of bismuth compounds after intravenous injection and the fact that there is less of a "depot" action such as occurs after an intramuscular injection of the drug. This is a disadvantage of bismuth compounds administered intravenously compared with intramuscular administration. It therefore appears that weekly intravenous injections of bismuth compounds, provided no other treatment is given, are not sufficient in the treatment of patients with early cases of syphilis. Lapsing treatment when bismuth

compounds are injected intravenously is probably more likely to cause a greater incidence of neurorecidive than would occur following irregular or lapsing treatment when bismuth compounds are administered intramuscularly.

In a previous study on intramuscular injection of bismuth compounds in the treatment of patients with syphilis, the following statement was made: "A few injections of arsphenamine and the cessation of all other treatment inhibit the consummation of immunologic responses of the host to the parasite, and doubtless produce a condition analogous to that existing in the primary incubation period, in which there are spirochetes and no immunologic reaction."

Bismuth compounds, on the other hand, by reason of less energetic spirocheticidal action than arsphenamine and perhaps by virtue of intramuscular administration, in all probability does not inhibit immunologic reaction of the host to such an extent as it is believed that arsphenamine does. One would, therefore, expect a lessened incidence of early neurosyphilis following irregular and lapsing treatment with bismuth. In the light of a much greater experience with the intramuscular use of bismuth compounds in the therapy of syphilis, this statement is still pertinent.

In the therapy of syphilis, intramuscular treatment offers many advantages over intravenous treatment. The therapeutic action following intramuscular treatment is less energetic but more prolonged. Moreover, intramuscular treatment is a safer procedure, since it is a less toxic route, and since there is lessened incidence of acute untoward reactions. In the spirochetemia stage of early syphilis, however, intravenous therapy is more desirable in view of its more effective action; indeed, it is the systole in the therapy of early syphilis—the "heavy artillery" action in the sense of Ehrlich and the "punch" action in the sense of Felke.

STATUS OF INTRAVENOUS BISMUTH THERAPY

The status of bismuth compounds administered intravenously in the therapy of syphilis is shown in the following: The injection of drugs into the circulation should not be practiced indiscriminately. Bismuth compounds are more toxic when administered intravenously than when administered intramuscularly. The amount of a single injection of bismuth compounds should not exceed 0.05 Gm. of the metal; injections of more than this amount are of questionable safety. It may here be recalled that 0.2 Gm. of a bismuth preparation, high in bismuth content, is uniformly well tolerated when injected intramuscularly. Bismuth compounds injected intravenously may produce albuminuria. When intravenous injections of bismuth compounds are used alone in the treatment of patients with early syphilis, weekly injections are probably insufficient.

It is of importance that treatment be continuous. Indeed, it is doubtful whether treatment of a patient with early syphilis solely with bismuth compounds administered intravenously is justified.

Considering the greater toxicity of the drug when administered intravenously, which necessitates limitation of dosage, and its rapid excretion, it is doubtful whether the intravenous route is more effective in the therapy of syphilis than the intramuscular route. A possible exception is the following circumstance: By reason of the greater spirocheticidal action of bismuth compounds injected intravenously, such injections may find a place in the therapy in early cases of syphilis in conjunction with other therapy, particularly in patients intolerant to arsenic. In such patients the use of both intravenous and intramuscular injections with bismuth compounds doubtless offer more in therapeusis than bismuth compounds administered only intramuscularly. Again, in patients other than in the acute early stage of syphilis, as for example "Wassermann-fast" patients, the administration of bismuth compounds intravenously may be of some value; however, this phase of intravenous administration of bismuth compounds was not investigated in this study.

1934 Spruce Street.

ABSTRACT OF DISCUSSION

Of Papers by Drs. McBride and Dennie, Elliot and Todd, Stillians, Morrow and Epstein, and Schamberg and Rule

Dr. Udo J. Wile, Ann Arbor, Mich.: It is gratifying that Dr. Dennie brought out the importance of potassium iodide in spite of all the various newer drugs now being used. I think that view meets with sympathetic response from all who have had much to do with syphilis, and who by reason of a large material carry the burden of trying out new remedies. My own experience has been that after I have tried everything else, mercury and iodide seem to form the background of treatment.

Dr. Schamberg's paper was interesting in view of the belief that is held in some quarters that the innovation in paretic therapy is not due so much to the fact that the patients are given another infection, but is the result of the febrile condition in connection with the new infection. I might say that the fact of the major factor of heat is borne out by the experiments that are being carried out with relapsing fever as well as by the other types of *Spirillum* infection, and with one human experiment, which proved definitely the effect of fever on the syphilid. While the febrile reaction of relapsing fever is not so great as in that with malaria, the therapeutic effects are not so good as when the pyrexia approaches the limit of tolerance for man, from 105 to 106 F. A young woman who had four large chancres at the introitus was given the malarial treatment and no other treatment for from two to four weeks. A careful examination was made of the lesions every day, and within forty-eight hours spirochetes could not be demonstrated. Within from four to five days all the lesions subsided, much more rapidly than could have been possible by any other method. While the

spirochetes had disappeared, the patient's Wassermann reaction was not affected in the least, and it was necessary to institute other forms of treatment.

Dr. Elliott's case of hepatitis is extremely interesting and valuable and, I think, bears an important lesson. Most of these patients who develop hepatitis early do so because of a preexisting damage to the liver. This is borne out by the patients who have been shown to have an old underlying hepatitis which may be due to some previous infection during their life, in which actual jaundice did not occur but damage to the liver did.

I have seen only two cases of syphilitic phlebitis such as Dr. Morrow described, and I think this is due to the fact that the late damage to the blood vessels so often seen is due to the fact that this seldom occurs in veins, and that is why it is seen only rarely.

Dr. Hermann Goldenberg, New York: I find a corroboration of Dr. Schamberg's animal experiments in a paper which has been recently published from the dermatologic clinic in Prague, a preliminary report of the work in which the experimenters used the Rocky Mountain spotted fever virus which, when injected into a male rabbit, causes a fever of a continuous type, ranging from 104 to 106, lasts for from seven to ten days and disappears spontaneously. The authors took male rabbits with different stages of syphilis and injected them with the virus of Rocky Mountain spotted fever. The influence on syphilis was controlled by transmission of the popliteal glands and by experiments of reinfection. The authors reached the conclusion that in four cases there was a probable cure and in one a positive cure. A detailed report of their experiments will be forthcoming in the near future in the Archives of Dermatology and Syphilology.

Dr. C. Morton Smith, Boston: It is interesting to know that Dr. Dennie has reached the conclusion regarding the newer remedies that Dr. Oliver Wendell Holmes voiced many years ago in quoting Pope: "Be not the first by whom the new are tried, nor yet the last to lay the old aside."

Regarding the Wassermann reaction in pregnancy, it is interesting that Dr. Stillians has found almost the same proportion of positive reactions that we did at the Massachusetts General Hospital. The average percentage at the Lying-In Hospital is from 5 to 6. In lower social strata and in other parts of the city, it rose to 10 per cent, and in groups made up of colored women it reached as high as 30 or 35 per cent.

The question of false positive reactions is always more or less of a bugaboo. During the war, Dr. Hinton of the Massachusetts State Laboratory did the routine Wassermann tests on all applicants for naval aviation. Their ages were between 18 and 28, and he found less than one half of 1 per cent of positive Wassermann reactions in this group. In the absence of a history of infection and physical signs of syphilis, this rate could be taken as an average for false positive reactions.

Dr. Paul A. O'Leary, Rochester, Minn.: I have continued the clinical study of the patients with neurosyphilis treated by malaria therapy to note the influence of temperature as well as the presence of *Plasmodium vivax* in producing the beneficial results. In previous communications I called attention to the fact that the outstanding therapeutic effects are to be noted in the patients who developed a high temperature, who retained the fever the longest and who had twelve or more chills. Our further observation during the past two years has confirmed this impression. There have been eighteen patients in our entire series who aborted the malaria spontaneously after eight or more chills, and in this group the therapeutic effects were in proportion to the height of the temperature and the

number of the chills. In a few, who spontaneously stopped the chills and fever after two or three fever bouts who maintained *Plasmodium vivax* in the blood stream for several weeks thereafter, slight, if any, improvement was to be noted. So, from a clinical investigation, it would seem that the fever itself was the paramount factor in producing the clinical improvement in parenchymatous neurosyphilis. It is, however, worthy of comment that up to this time the percentage and the degree of remission in general paralysis have not been as pronounced from the use of other fever-producing agents such as *Spirochaeta refringens* and typhoid vaccine as have been the results from malaria therapy.

Dr. Elliott's paper emphasizes the value of determinations of bilirubin as applied to one phase of syphilotherapy. I have also had the opportunity to study the liver functional tests in a patient with hepatic disease which developed during the secondary phase of syphilis, and found that estimations of the bilirubin index afforded a valuable guide in treatment. It is a great misfortune that so little is known about hepatic function and hepatic disease in general, and of course until the knowledge in regard to the former is increased, the value of any liver functional test will be limited. In late syphilis of the liver, the estimates of bilirubin do not indicate the degree of gummatous or diffuse hepatitis present unless the involvement is so extensive that the hepatic function is materially curtailed. However, in the acute toxemias of the liver with clinical evidence of impaired function, the bilirubin estimates do indicate the presence of hepatic dysfunction.

Dr. Charles Williams, New York: Dr. Morrow's paper was interesting in showing syphilis in the veins in the secondary stage, and I wish to call attention to the syphilis in the veins during the tertiary stage. The eruption so produced is referred to as livedo racemosa and is often reported in the German literature.

Dr. Schamberg's paper was interesting, and I wish to call attention to what I think is the earliest treatment of syphilis by malaria which I came across in my reading recently. The patient was Benvenuto Cellini, who states in his autobiography that he acquired syphilis and treated himself with a guaiac and a course of diet, etc. He improved, but after he stayed out in the marshlands the disease returned with fever. He again followed his line of treatment by means of guaiac and diet, and after fifty days his health was reestablished. The evidence is flimsy, to be sure, but it is at least possible that the fever was due to malaria and was the real cause of his cure.

Dr. Schamberg: I am sure that Dr. Klauder would not wish the impression left that he favors the intravenous use of bismuth. I think his work definitely indicates that bismuth is a spirocheticide, a view which I have held for some time. As I recall, within twenty-four hours after the administration of bismuth spirochetes have disappeared from lesions. Dr. Wright has observed in our clinic the disappearance of spirochetes from a condyloma in an infant forty-eight hours after the administration of bismuth. This is comparable to the results obtained with arsphenamine. I think the more experience one has with bismuth, the more valuable one will find it.

Dr. Klauder: Time did not permit me to state my conclusions as to the status of bismuth administered intravenously in the therapy of syphilis. Such conclusions are stated in the completed paper. I may briefly state that I do not believe intravenous injections of bismuth should routinely displace the intramuscular route. The drug administered intravenously exerts a more energetic therapeutic action than intramuscular injections; at the same time, it is more toxic, which necessitates a restricted dosage. Intravenous injections of the drug may find a place in treatment of early syphilis in conjunction with other

treatment, particularly in patients with early syphilis, who are intolerant to arsenic. In these patients, bismuth both intravenously and intramuscularly offers much more than bismuth intramuscularly alone. Dosage within 50 mg. of the metal bismuth I regard as safe and believe one is justified in administering it in selected cases. On the whole, knowledge relative to the administration of bismuth intravenously is a valuable addition to the therapeusis of syphilis.

FUNGI AND FUNGOUS DISEASES

LECTURE III *

ALDO CASTELLANI, C.M.G., M.D.

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NEW ORLEANS

(Concluded from page 220)

SKIN DISEASES DUE TO FUNGI

PRURITUS ANI AND PRURITUS VULVAE OF MYCOTIC ORIGIN

Mycotic Pruritus Ani

Some years ago, I described as a separate entity "Pruritus Ani of Mycotic Origin." My publications attracted little attention, and even in recent articles on pruritus ani by various authorities the mycotic or fungal variety is not mentioned, although the so-called bacterial type (streptococcus pruritus ani) is often discussed.

It may perhaps be of advantage to give a brief general account of the condition, incorporating into it the result of my further researches on the subject.

Definition.—Mycotic (phycotic) pruritus ani is a form of pruritus ani caused by higher fungi than bacteria (mycetes, higher fungi) generally fungi of the genus *Epidermophyton,* the same fungi which cause pruritus interdigitalis pedum (toe phytosis, dermatitis interdigitalis mycotica, mango toe) and also ordinary dhobie itch or tinea cruris. The condition is, in fact, as a rule, one of latent epidermophytosis of the perianal region, without the presence of the usual objective symptoms of an ordinary active epidermophytosis.

Synonyms.—Phycotic pruritus ani, mycetic pruritus ani, mycotic pruritus ani, fungal pruritus ani, pruritus ani due to higher fungi, epidermophytic pruritus ani.

Clinical Symptoms.—The patient complains of severe pruritus, not as a rule continuously, but at intervals. The pruritus is often worse at night, but the attacks of unbearable itching may come at any time. Inspection of the anoperianal region in recent cases may reveal nothing at all except perhaps signs of scratching, but in most cases on careful examination, minute, red, slightly raised, infiltrated patches may be seen in the perianal region, occasionally arranged into two curved lines. In a number of old cases signs of an eczematous dermatitis, due to

scratching, are present, and streptococcus and other secondary bacterial infections may become engrafted on the mycotic condition.

When the secondary bacterial infection becomes abundant, especially if many coli and proteus germs are present, the fungus may disappear completely or become extremely scarce. In some old-standing cases, the skin is thickened and lichenified.

ILLUSTRATIVE CASES

CASE 1 (Uncomplicated type).—This case has already been published by me in the *Journal of Tropical Medicine*. The patient, a Ceylon planter, came to consult me in October, 1924. He had been suffering from anal pruritus for six years and tried numerous ointments and lotions without any permanent benefit. He denied ever having had dhobie itch or mango toe (dermatitis interdigitalis pedum). With the exception of a few minute red patches which did not give the impression of an epidermophytic infection, found on close examination, nothing abnormal was observed in the anoperianal region. Scrapings were made every other day for two weeks, and examined microscopically in solution of potassium hydroxide; they were always negative except on one occasion, when a few spores and portions of mycelial threads were seen. After many failures, a fungus was grown with all the characteristics of *Epidermophyton cruris*. An ointment containing salicylic acid, eucalyptus oil, mercury salicylate and bismuth subnitrate (Deek's ointment) cured the condition.

CASE 2.—Mr. A. G., aged 40, who had never been out of Europe, came to consult me in February, 1925. Six years previously he began complaining of pruritus ani after a sojourn of several months in the south of France. He was treated with various ointments without any distinct benefit. At the time he consulted me, the skin about the anus was red and somewhat thickened. Inspection of the inguinal-crural region showed absence of dhobie itch and the patient denied ever having had it. On questioning him, I elicited the fact that he had been suffering frum pruritus interdigitalis pedum for several years; inspection of the toes showed a few cracks and slight peeling. From scrapings of the toes I obtained *Epidermophyton cruris* fairly easily, but scrapings from the anoperianal region, made and examined daily, remained negative for nineteen days, when a few mycelial segments of a fungus were found. The fungus was grown with great difficulty owing to the presence of numerous cocci and bacilli; it was *E. cruris*. In this case the conditon responded satisfactorily to a sulphur salicylic ointment and a tar compound.

CASE 3.—Mr. N. B., aged 25, has been in the Far East for three years. He consulted me in November, 1924. Two years previously he had dhobie itch, which he said was cured by means of a Goa powder ointment. For six months previous to the time I saw him he had severe pruritus ani. Examination of the anoperianal region showed nothing except signs of scratching. After many attempts *E. cruris* was grown.

Etiology.—The cause of the condition is generally found in the presence of the fungi of the genus *Epidermophyton*, the same fungi which produce ordinary tinea cruris (dhobie itch) and pruritus interdigitalis pedum; occasionally, fungi of the genus *Trichophyton* may be present. The species of epidermophyton found have been *E. cruris* and *E. rubrum;* yeastlike fungi also are often present, but I doubt whether

they play an important etiologic rôle. The botanic characters of epidermophyton fungi, trichophyton fungi and yeastlike fungi have been given in lecture I.

Yeastlike Fungi

In some cases of pruritus ani I have found fungi of the genus *Monilia* Persoon and other yeastlike organisms (saccharomyces, cryptococcus, etc.), either alone or together with *Epidermophyton,* but I doubt whether they play an important part in the causation of the pruritus; they probably play the rôle of secondary invaders, similar to the rôle played by certain bacteria, such as streptococcus. In a recent case there was present a most peculiar fungus, somewhat yeastlike, but gram-negative, which produced in hanging-drop cultures mycelial elements of most different shapes, which might be called *Cryptococcus multiformis.*

Bacteria

Bacteria are usually present, and coli-like organisms, proteus and various cocci, including several kinds of streptococci, have been found. I have found, also, some peculiar, yellow, pigment-producing bacilli (*B. metaflavus*). They may, and probably do, play a part in the causation of the secondary eczematous dermatitis, but I doubt whether they alone can produce severe pruritus. A case of so-called streptococcus pruritus recently seen by me turned out to be a case of epidermophyton infection, due to *Epidermophyton cruris.* The streptococcus was abundantly present, but was not the actual cause of the pruritus, as streptococcus vaccine did not cause any improvement in the local condition, while an antimycotic treatment with sulphur and salicylic acid cured it.

Diagnosis.—A definite diagnosis of mycotic pruritus ani cannot be made without epidermophyton or trichophyton fungi being found microscopically or by mycologic cultural methods; a diagnosis of probability can often be made, however, on clinical grounds, the minute, red, infiltrated patches, fairly often seen on careful examination in the anoperianal region, being suggestive, especially if the patient is suffering from mycotic dermatitis of the toes, or gives a history of having suffered from dhobie itch or tinea cruris in the past. When the bacterial flora is abundant it may be extremely difficult or impossible to isolate the fungi.

Course and Prognosis.—The course of the condition is chronic, but periods of great improvement and apparent cure may alternate with periods of severe recrudescence. Attention should be called to certain cases, fortunately rare, in which although the fungus under appropriate treatment has completely disappeared, the pruritus continues. This is observed in highly strung, nervous persons. Difficult cases are also

encountered in patients suffering from, or having a tendency to, true eczema; when they become infected with epidermophyton fungi—either the irritation caused by the fungi themselves or that set up by the treatment to eradicate the condition—an attack of eczema may develop not only in the anoperianal region but also in many other regions of the body.

Treatment.—In uncomplicated cases an ointment I have found efficacious is the following: precipitated sulphur 30 grains (1.95 Gm.), salicylic acid 30 grains (1.95 Gm.) and petrolatum 1 ounce (31 Gm.)—the ointment I introduced some years ago for the treatment of ordinary tinea cruris. A preparation that frequently serves remarkably well is Deeks' ointment, which consists of salicylic acid 4 parts, bismuth subnitrate 10 parts, mercury salicylate 4 parts, oil of eucalyptus 4 parts, petrolatum and wool fat sufficient to make up to 100 parts. It is interesting to note that long ago Deeks found that this antimycotic ointment had a beneficial action in many cases of pruritus ani, although the existence of a mycotic type of the condition was not known at the time. A slightly modified Whitfield's ointment is also useful: phenol 5 grains (0.3 Gm.), salicylic acid from 15 to 30 grains (1 to 1.95 Gm.), benzoic acid from 15 to 30 grains (1 to 1.95 Gm.) and petrolatum 1 ounce (31 Gm.). In several cases I have found the following ointment most useful: tar ointment 1 drachm, zinc oxide 4 grains (2.6 Gm.), salicylic acid ointment 4 drachms and wool fat to make 1 ounce (31 Gm.). In certain cases I have found that painting the parts with carbofuchsin is most efficacious.

In some cases an ointment containing 2 grains (0.13 Gm.) of chrysarobin to the ounce of petrolatum is efficacious, but it may occasionally induce a severe reaction, and, of course, it stains the underclothing. It should not be used when there is any disease of the kidneys, and the patient should be told never to touch his face or eyes after applying the ointment.

Diluted tincture of iodine is at times useful. A strong lotion of potassium (15 grains [1 Gm.] to 1 drachm to distilled water 1 ounce [31 Gm.]) is occasionally useful, also the frequent swabbing of the anoperianal region with a perchloride of mercury lotion (1 in 1,000) or resorcinol lotion (1 to 5 per cent).

When the pruritus is unbearbable, painting the parts with a lotion consisting of silver nitrate 15 grains (1 Gm.) and spirit of ethyl nitrite 1 ounce (31 Gm.), at times stops the itching, either immediately or after a short time, during which the pruritus may become intensified; this paint should be used with care. In chronic cases roentgen-ray treatment is to be recommended; it is often successful, though, unfortunately, not always.

MYCOTIC PRURITUS VULVAE

This condition is similar to pruritus ani of mycotic origin, and it is not rare to observe female patients suffering from both conditions.

Etiology.—Mycotic pruritus vulvae is usually caused by the presence of fungi of the genus *Epidermophyton,* occasionally of the genus *Trichophyton,* which remain dormant in the external region of the labia majora without giving rise to the ordinary signs of active tinea cruris or dhobie itch. Not rarely, yeastlike fungi, usually of the genus *Monilia,* but occasionally belonging to the genera *Cryptococcus, Saccharomyces* or *Endomyces,* may also be found—the fungi of the vaginal as well as oral thrush—but in my experience it is rather doubtful whether they can alone give rise to severe pruritus, as under an appropriate treatment monilias may be made to disappear, but the pruritus persists in most cases. Monilias probably play the rôle of secondary invaders similarly to the many bacteria so often found in the condition, among which are various cocci and coli organisms.

Clinical Symptoms.—The patient complains of severe pruritus, in most cases at intervals. The examination of the genital parts may reveal nothing at all, but at times a few minute, red, hardly raised infiltrated patches may be seen on the external surface of the labia majora and perineum. In long-standing cases an eczematous moist or dry dermatitis often develops, as a result of secondary bacterial invasion. In chronic cases there is often also a large amount of vaginal discharge, in which various bacteria are found and frequently monilia fungi.

ILLUSTRATIVE CASE

An elderly spinster consulted me some time ago on account of vaginal pruritus of some years' duration, for which different medical men had administered various treatments without any distinct amelioration. In the perianal region, on the perineum and on the labia majora, a few small reddish patches were seen, which it was thought might be due to scratching. There was an abundant purulent discharge from the anus, with symptoms of proctitis. A complete mycologic and bacterial investigation was carried out. From the scrapings of the perianal region and the labia majora a fungus was grown with the characters of *Epidermophyton cruris* Castellani, 1905, the fungus which is the commonest cause of dhobie itch and pruritus interdigitalis pedum. In the vaginal and in the rectal discharge enormous numbers of monilias were present, with few bacilli; cultivation showed the fungus to be a strain of *Monilia pinoyi.*

The following treatment was given: Creosote was administered by mouth; tincture of iodine, which in this case did not give rise to any local pain or irritation, was freely applied once a day to the anoperianal region, the perineum and the external surface of the labia majora. For the first three days hot alkaline irrigations (1 drachm of bicarbonate of soda to a pint of water) were given; afterward, twice a day, an iodine irrigation (tincture of iodine 1 drachm, water to make 2 pints). Within two weeks the patient was completely free from the anal and vaginal pruritus; the purulent rectal discharge decreased, but did not quite disappear. The monilias present diminished enormously in number, but did not disappear completely.

Prognosis.—The condition does not have a tendency to spontaneous cure, but periods of great improvement and even complete cessation of the pruritus may be noted.

Fig. 23.—Tinea imbricata (Tokelau).

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Treatment.—This is on the same lines as for mycotic pruritus ani. In uncomplicated cases my salicylic sulphur ointment (salicylic acid 30 grains [1.95 Gm.], sulphur 30 grains [1.95 Gm.] and petrolatum 1 drachm), Deeks' ointment half strength, a modified Whitfield ointment, or painting with diluted tincture of iodine or carbolfuchsin give satisfactory results. When an acute eczematous dermatitis, generally due to vaginal discharge, is present, local applications with solution of lead subacetate (1 drachm to the pint) and coal tar solution (2 drachms to the pint) are useful, and vaginal douching with iodine (tincture of iodine 1 drachm to two pints) or potassium permanganate (1 in 5,000) should be carried out. Later, tar ointments or pastes, such as pine tar from 10 to 20 minims, zinc oxide 2 drachms and petrolatum to make 1 ounce (31 Gm.), are useful. Roentgen-ray treatment is at times useful.

TINEA IMBRICATA

(Tokelau)

Historical.—This dermatomycosis, which is extremely common and of great practical importance in certain tropical countries, was first described by Dampier in his book, "A Voyage Round the World," in 1789. In Alibert's "Atlas of Skin Diseases," published in 1832, there is a good illustration depicting the disease. In 1874, Tilbury Fox gave a description of the complaint under the term Tokelau ringworm. He detected in scales a filamentous fungus and considered it to be identical with the fungus of European ringworm. At that time discussion began and continued for many years on the subject whether the disease was a separate entity or merely European ringworm modified by the different climatic conditions. The great majority of the European authorities, who, however, had not had personal experience with the malady, were opposed to considering the disease a separate one, while the medical men practicing in the tropics generally believed it to be a different condition from ringworm. Valuable researches were carried out by McGregor in 1870 and Coniger in 1871, but Manson's researches in China during the period 1879-1882 are by far the most important. He described the eruption in a masterly manner, and first introduced the appropriate name of tinea imbricata. Moreover, he gave a good microscopic description of the fungus, although, as might be expected, using the technic of that time, he did not succeed in cultivating it. He considered it to be a non-cultivable trichophyton for which Blanchard suggested the name *T. concentricum.* In recent years the malady has been generally considered to be a form of aspergillosis. In 1910-1911 I investigated the disease in Ceylon, and proved that the aspergillus and aspergillus-like fungi have nothing to do with the disease, and that when they are present in the scales, as they often are, they are merely saprophytes or contaminations.

By using a special technic I succeeded in growing the fungi which I consider to be the true causative agents of the disease, and for which I created the genus *Endodermophyton* (see etiology).

Synonyms.—A remarkable thing is the large number of synonyms in existence to designate the disease. These may be grouped as follows:

(*a*) From the name of the countries where the condition is common; for instance, "Tokelau" is the name of a Pacific island in which the malady is rife; "Tamana" is the name of another island of the Gilbert group.

(*b*) From the name of the patient who first introduced the disease in certain countries. Turner states that at one time the disease in the island of Tokelau used to be known as "Le Pita" from "Peter," the name of the native of Tamana who in 1850 introduced the disease into Tokelau.

Fig. 24.—Endodermophyton tropicale—dextrose agar culture.

(*c*) From certain clinical appearances: "tropical ichthyosis," an unfortunate designation as true ichthyosis is far from rare in the Tropics; herpes farinosus (Ritter); herpes desquamans (Turner); dermatomycosis chronica exfoliativa (Tamson); tinea imbricata (Manson).

(*d*) From the generic name of the fungus supposed to be the causative agent: aspergillosis of Wehmer, lepidophytosis of Tribondeau.

(*e*) From the names of the authors who have more completely investigated the malady, for instance, "Turner's herpes" and "Manson's herpes," the term herpes being used by Roux and others in the obsolete meaning of mycotic disease.

(*f*) Terms of unknown origin; for instance Gugo, Cascado, Buckwar.

Geographic Distribution.—The disease is common in many of the Pacific Islands, in southern China and in the Malay States, and in recent years it has spread to Ceylon and southern India. Cases have been reported from South Africa and South and Central America, but some doubt has been expressed as to their having been true tinea imbricata.

Etiology.—The etiology of this disease has been the subject of much controversy until recently. As I have already mentioned, Tilbury Fox in 1874, examining microscopically scales sent to him from the Tropics,

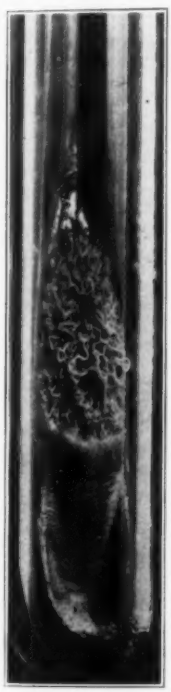

Figure 25

Figure 26

Figure 27

Fig. 25.—Endodermophyton tropicale—dextrose agar culture (very old).

Fig. 26.—Endodermophyton tropicale—dextrose agar culture.

Fig. 27.—Endodermophyton indicum.

noted the presence of a fungus which he considered to be identical with the fungus of European ringworm. I have consulted his original paper: the drawings of the fungus suggest that he was in all probability dealing with an aspergillus, which contaminated the scales, as is often the case. In 1879 and following years Manson described the fungus as a trichophyton, which he did not succeed in cultivating. Blanchard considered it a noncultivable trichophyton and called it

T. concentricum. Later, principally owing to the investigations of Tribondeau and Wehmer, the opinion became general that the disease was a form of aspergillosis. Tribondeau described fructification slightly different from those of an aspergillus and created the genus *Lepidophyton* (λέπις = scale, ψυτόν = plant); Wehmer described it as a true

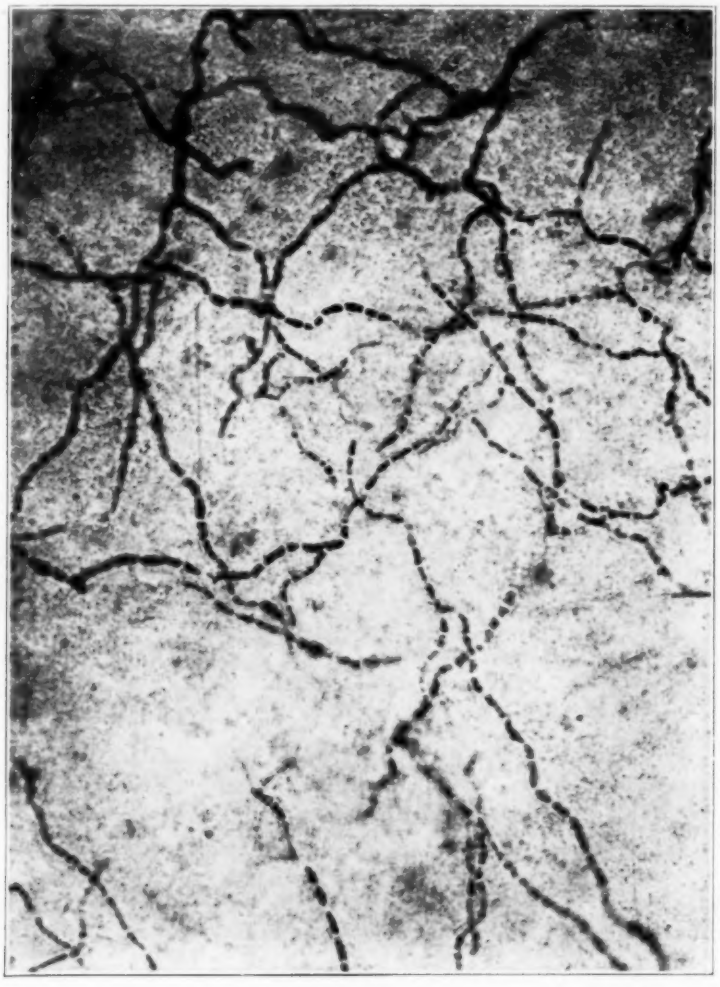

Fig. 28.—Tinea imbricata; fungus in scale.

aspergillus: *Aspergillus* Tokelau. In 1910 and 1911 I investigated the malady in Ceylon and came to the conclusion that the aspergillus-like fungi are merely secondary invaders or contaminations. By using a special method I succeeded in growing the causative fungi as proved by the successful reproduction of the disease in volunteers when pure cultures were used.

To designate these fungi, I created the genus *Endodermophyton.*

The fungi belonging to the genus *Endodermophyton* are characterized by their growing between the superficial and deep layers of the epidermis, forming an interlacing felt of mycelium which detaches the horny and granular layers from the rete malpighii. They do not invade the hair follicles and do not cause suppuration. Their cultures are somewhat similar to those of the genus *Achorion.*

The difficulty in growing these fungi artificially is explained by the fact that they do not grow on solid mediums direct from the scales. These, after being treated with alcohol from five to ten minutes, must be placed in dextrose broth tubes, one scale in each tube. Most of the tubes become contaminated with bacteria, but in those that remain clear, after a time, from five to ten days, a few delicate short mycelial filaments will be seen originating from the scales. The growth slowly increases until after a few weeks it takes the appearance of a small white fluffy

Fig. 29.—Tinea imbricata.

mass with a dark spot (the scale) in the center. The fungi can then be transplanted on solid mediums, on which they will grow quite well, and can be subcultivated indefinitely. The various species may be differentiated as follows:

1. Dextrose agar cultures, amber colored; duvet, absent or present only in slight amount—*tropicale.*
2. Dextrose agar cultures, deep orange, pinkish or red; white duvet often present—*indicum.*
3. Dextrose agar cultures after some weeks become black—*concentricum.*
4. Black pigmentation rapid—*mansoni.*

Experimental Reproduction.—Using pure dextrose agar cultures, I have succeeded in experimentally reproducing the disease in natives who had volunteered. The cultures must be fairly recent; old cultures lose their pathogenicity or merely give rise to an evanescent papuloid tricophytic-like eruption.

Predisposing Causes.—As regards age, in my experience young adults mostly are affected, but children and old people may contract the disease. Men are infected much more frequently than women. It is doubtful whether there is any racial disposition. In Fiji it is said, however, that the immigrant Tongas rarely contract the malady, while the indigenous Fijians are extremely prone to it. Some authorities believe that this relative immunity is due to the Tongas' habit of anointing their skin.

As regards climatologic influences, Manson has made the interesting observation that tinea imbricata is rife especially in those tropical coun-

Fig. 30.—Experimental tinea imbricata (Endodermophyton tropicale).

tries and districts in which the climatic conditions are favorable for the growth of the coconut tree. I can confirm Manson's observation. In Ceylon tinea imbricata is not very common, but the cases one sees generally come from the coconut districts. There is not any doubt that a hot moist equable climate is the most suitable for the fungi of tinea imbricata, as it is the most suitable for the growth of the coconut tree.

Clinical Symptoms.—The development of the eruption is most interesting. At the beginning one or several small roundish or oval dark brown small spots appear, generally on the arms, chest or back. After a short time each brownish spot splits in the center, and in this way a ring of flaky large scales attached at the periphery is formed; this scaly

ring expands peripherally, and while it does so another brownish spot appears in the center in the same site as the first brown spot; this new brown patch also breaks in the center, and in this way a second scaly ring is formed, which expands toward the periphery inside the first ring; again in the center a dark patch appears, which splits, and a third ring is formed inside the second; and so on until a number of scaly rings develop. Sir Patrick Manson has aptly compared this development of concentric rings to the concentric ripples produced by a pebble thrown into a pool of water, and when the eruption starts from many points, as is often the case, owing to auto-inoculation, it is as if a shower

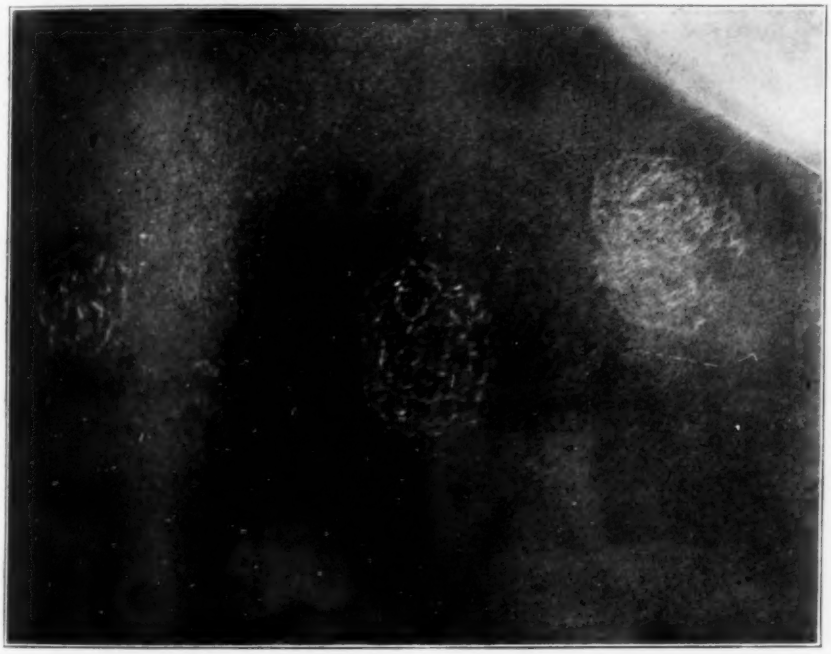

Fig. 31.—Experimental tinea imbricata (Endodermophyton indicum).

of pebbles had fallen in the pond, and many systems of spreading rings that intersect each other in various ways are produced.

The scales are flaky, tissue paper-like, large, up to half an inch in length, dry and dirty grayish or brownish. The fungus never invades the hair follicles, nor, according to some authorities, the nails. I must say, however, that in my experience the nails are often affected, becoming discolored and brittle, and this has also been Manson's experience.

The eruption does not at first have much effect on the general health of the patient, but the pruritus it induces is really terrible, and the native patients refuse to do any work, remaining in their compounds, where they can be seen squatting or lying down and scratching their bodies

the whole day. I have noticed that the itching is greatly increased by certain diets: for instance, the dry fish diet often given in Ceylon hospitals makes the pruritus absolutely unbearable.

Clinical Varieties.—A variety fairly frequently encountered is the diffuse type without concentric figuration. The scales, however, are

Fig. 32.—Tinea imbricata.

typical and identical with those found in the concentric type. The same fungus may cause at times the concentric type and at others the diffuse type. In certain cases, however, the lesions caused by the different fungi seem clinically to be somewhat different; the lesions caused by *E. indicum* seem in certain cases a little more superficial than those caused by *E. tropicale*, and the scales are not situated so close together.

Diagnosis.—The clinical picture of the disease is most characteristic, even when the eruption is of the diffuse type. The large dry tissue paper-like scales overlapping each other like tiles on a roof are typical, but the diagnosis is certainly difficult to the newly arrived European medical man, who may never have heard of the disease. On superficial

Fig. 33.—Tinea imbricata.

examination the malady does not strike one as being of epiphytic origin, and the cases I generally had in the Colombo Clinic were often diagnosed by visitors—and naturally so—as cases of ichthyosis or of pityriasis rubra; in fact, it is interesting to note that one of the many synonyms of this malady is "tropical ichthyosis." Of course, microscopic examination of the scales will reveal the presence of an enormous number of mycelial filaments, and this will clear the diagnosis at once.

Prognosis.—The disease, as I have already stated, has not at first a serious influence on the health of the patient, but the condition is chronic, and after a time the patient not rarely becomes anemic, emaciated and a nervous wreck, owing to the continuous sensation of pruritus and loss of sleep. At any rate, the patient is not fit for any work; this is of great practical importance as it tends to decrease the labor force on plantations.

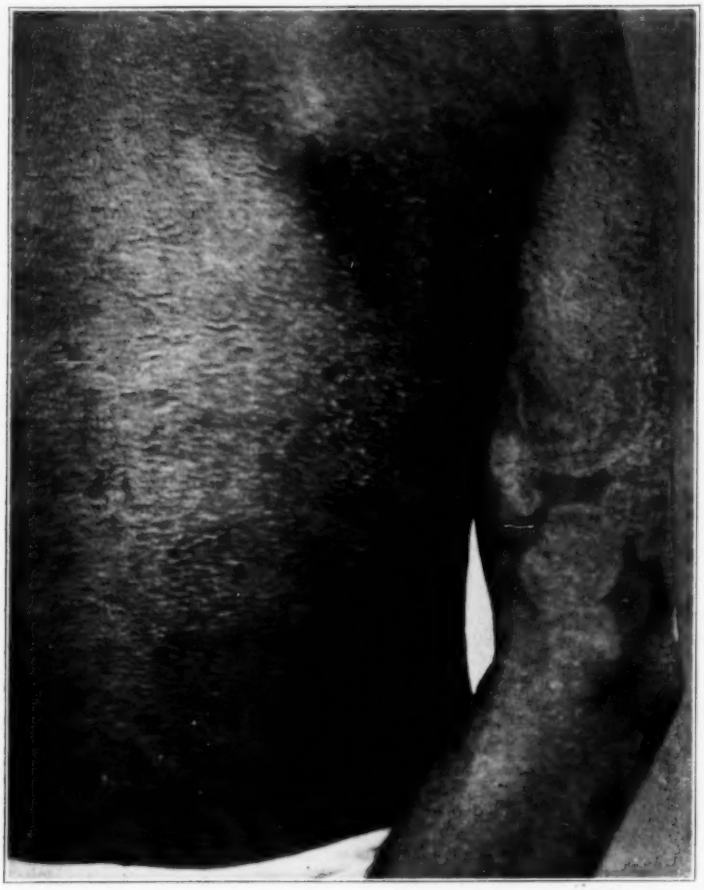

Fig. 34.—Tinea imbricata.

Treatment.—The disease never shows any tendency to spontaneous cure, and its treatment is most difficult, as every tropical practitioner well knows. It is easy enough to obtain a temporary improvement and even a disappearance of the eruption; but, as a rule, a few days after the treatment is discontinued the eruption starts afresh.

In the Colombo Clinic I experimentally tried the most different drugs and ointments and came to the conclusion that the best routine

treatment is with resorcinol dissolved in compound tincture of benzoin (resorcinol 2 drachms and compound tincture of benzoin 1 ounce [31 Gm.] or with chrysarobin ointment.

It is interesting to note that resorcinol in ointment or in alcoholic solution has practically no action and that compound tincture of benzoin

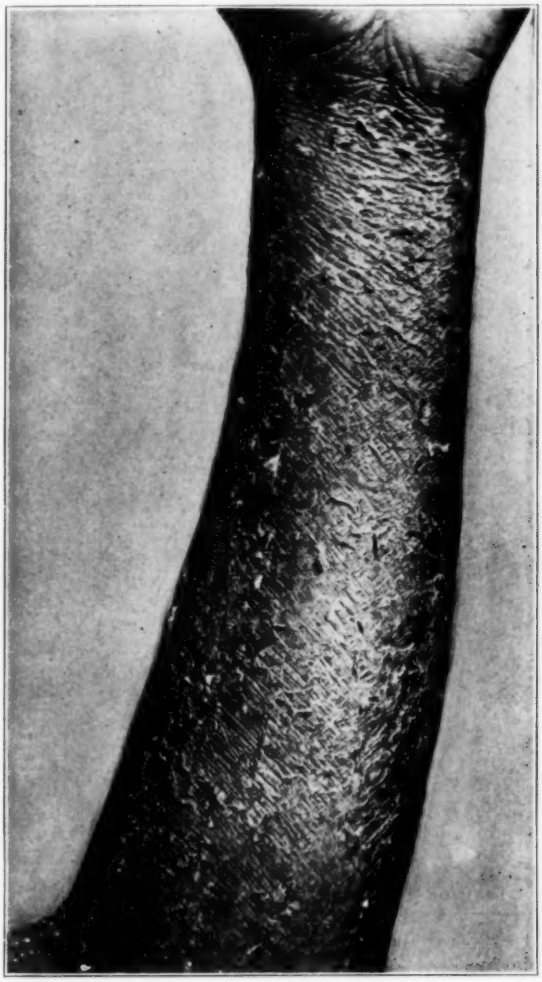

Fig. 35.—Tinea imbricata.

alone has also practically no action, but when the resorcinol is dissolved in the tincture good results are obtained. Tincture of iodine has little effect, but the old iodine liniment of the British Pharmacopeia is at times efficacious. Roentgen-ray treatment has been tried without brilliant result.

PINTA

(Carate)

In Honduras two years ago I saw more than a dozen cases of pinta, the diagnosis of pinta being confirmed by Dr. Urubuate, of Colombia, an expert on the malady. In Panama I saw two cases of pinta of Mexican origin thanks to the kindness of Dr. Connor and Dr. Bates.

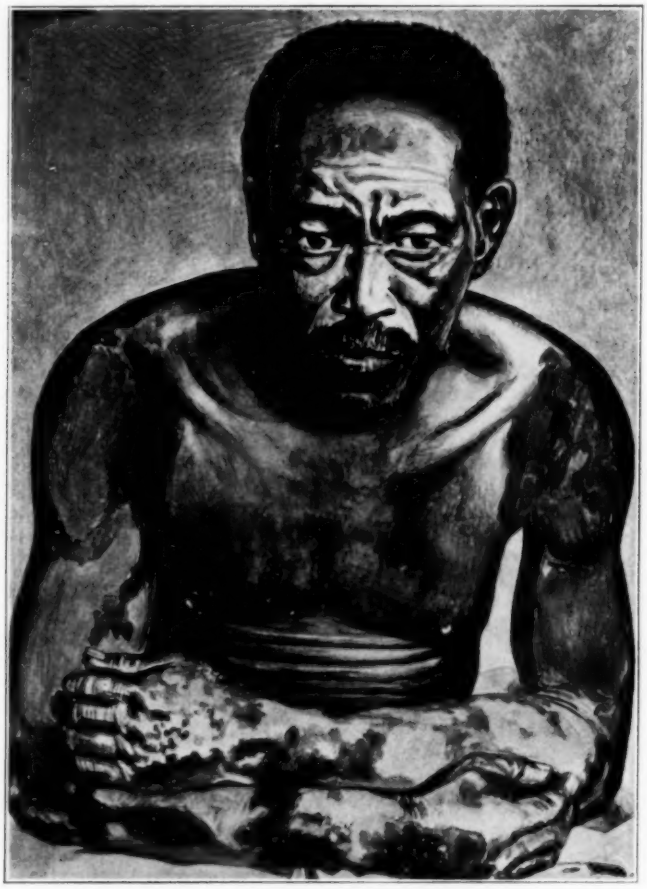

Fig. 36.—Pinta (from colored sketch).

Pinta is generally defined as a dermatosis characterized by patches of various colors, jet black, bronzine black, violet, red, yellow and white, and since the investigations of Ruiz Y. Sandoval and of Montoya the disease has been considered to be of mycotic origin. Ruiz Y. Sandoval believed that there was only one species of fungus and that the different colors of the patches were due to the different depths at which the fungus was growing. Montoya found a large number of different fungi belonging to the genera *Aspergillus* (*Aspergillus pictor*, etc.), *Penicillium*

(*Penicillium montoyai*, etc.), *Monilia* (*Monilia montoyai*, etc.) and also fungi with intermediate characters between these genera. According to him, the black, blue and violet patches are caused principally by *Aspergillus* fungi; the yellow variety by *Monilia* and *Aspergillus*, and the white variety by *Monilia*.

During my brief sojourns at Porto Castilla and at Panama, I examined several cases for the presence of fungi by microscopic and cultivation methods. I will quote the results obtained in four cases.

ILLUSTRATIVE CASES

CASE 1.—A negro boy, about 14 years of age, examined at Porto Castilla, Honduras, was shown to me as exhibiting a typical case of pinta. The diagnosis was confirmed by Dr. Urubuate of Colombia. On the face he had yellow patches which I suspected immediately to be tinea flava; on the chest were several other yellow patches, but with a somewhat different clinical appearance, smoother and with margins not so well defined. On the arms were yellow patches identical with those found on the chest; on the forearms black patches and white patches, not raised, smooth and resembling patches of simple hyperpigmentation (bronzine, chloasma-like) and depigmentation (leukoderma); on the dorsum of the hands, white leukodermic-like patches were present.

Microscopic Investigation.—1. Yellow Patches on Face: A fungus was present in large amount with the characteristics of the fungus of tinea flava (*Malassezia tropica*); numerous roundish spores were collected in clusters and some mycelial articles were present; it did not grow on dextrose agar. I have no doubt that these patches were patches of tinea flava, a condition I have briefly described at the beginning of this lecture.

2. Yellow Patches on Chest and Arms: A few yeastlike bodies of large dimensions were present, but no mycelial elements. A moldlike fungus was grown that I have not yet botanically determined.

3. Black and White Patches on Forearms: Microscopically a few large yeastlike bodies were seen, morphologically identical with those found on the surface of the yellow patches on the chest. The moldlike fungus grown seemed to be identical with that grown from the yellow patches on the chest, and those found on the black and white patches.

4. Normal Skin: Some large yeastlike bodies were present; a moldlike fungus apparently identical with that obtained from the yellow patches on the chest and the black and white patches on the forearms was grown.

CASE 2.—A negro, aged about 40, exhibited on the forehead and alae nasi hyperpigmented patches, some bronzine and others presenting a blue tinge (blue pinta); on the malar region, yellow patches, smooth and without definite margins; on the upper regions of the arms, diffuse yellow patches; on the forearms, greatly hyperpigmented patches (black), and on the wrists and hands, patches of depigmentation (white) surrounded by patches of hyperpigmentation. Dr. Banting made sketches of this patient for me.

Microscopic and Cultural Investigation.—Scrapings from the bronzine bluish patches on the face and alae nasi revealed a few yeastlike bodies. Identical bodies were found in the yellow patches on the chest and the black and white patches on the arms and hands. From various patches, and also from portions of the skin which seemed normal, the same fungus, which I have not yet identified, was

grown. I am not inclined to give any etiologic importance to this fungus, as its situation was superficial; moreover, after the skin was washed with soap and water and then alcohol applied no fungus was detected microscopically, or grown. Scrapings from the yellow patches on the arms contained masses of spores and mycelial elements with all the characters of *Malassezia tropica*. I do not doubt that these were patches of tinea flava.

Case 3.—A negro, aged about 50, presented patches of hyperpigmentation, bronzine and chloasma-like on the face; a small black patch slightly raised on the neck, and several leukodermic patches on the forearms and hands. On the legs and thighs were seen several clinically trichophytic patches, with marked hyper-

Fig. 37.—Pinta, Mexican patient (from Dr. Bates).

pigmentation of the skin. Before any scrapings were made all the patches were washed with soap and water and then alcohol. Fungi were not seen microscopically or grown in any of the hyperpigmented patches on the face and apigmented zones on the forearms. From the slightly raised patch on the neck, clinically different from the bronzine chloasma-like patches on the face, a fungus with the characteristics of *Cladosporium mansoni* was obtained in abundance. Scrapings from the patches on the legs showed the presence of a trichophyton-like organism which I did not succeed in cultivating.

Case 4 (Pinta of Mexican Origin).—Patches of different colors, bronzine black, yellow and white, were present all over the body. On the neck and upper region of the chest, typical ringworm lesions were seen. Scrapings in solution of potassium hydroxide from the various pinta patches revealed the absence of fungi. It must be noted that scrapings of the epidermis, even of normal persons,

on which solution of potassium hydroxide has been acting for a fairly long time often show a large number of oval or roundish formations which might be mistaken for spores or fungi. In any doubtful cases staining the preparation will clear the diagnosis. Cultivation showed the presence of at least three different species of molds. These three species were grown from every patch and also from portions of skin that seemed normal. Scrapings from the ringworm patches showed microscopically the presence of a typical trichophyton.

Controls.—Scrapings from three apparently healthy natives at Porto Castilla were examined microscopically and by culture methods. In two instances, microscopically, a few yeastlike bodies were found, which were identical morphologically with those observed in the cases of pinta. Culturally, several molds were grown which also seemed to be identical with those found in pinta. In the

Fig. 38.—Pinta, patient from Honduras.

third case, fungi were not present, either microscopically or culturally; only the usual cocci and *B. subtilis* were grown.

Comment and Conclusions.—My investigation of pinta, for lack of time, has been only preliminary, and therefore I do not desire to come to any definite conclusions, but I will tentatively state my impressions of the disease as seen in Honduras, as follows:

1. Yellow Pinta: This term covers at least two conditions. In one, a fungus with all the characteristics of *Malassezia tropica* is found in great abundance; in the other, either no fungus of any kind is found, or at times, microscopically, a few yeastlike bodies are present. The first condition is in reality tinea flava. In most cases one can make the diagnosis on clinical grounds; the mycotic yellow patches (tinea flava) are generally more sharply limited and may be slightly raised;

the nonmycotic patches are not raised and the borders are not usually so sharply defined. They represent, perhaps, a stage in a process of partial depigmentation, of trophic origin, a stage in the process of depigmentation from black to white, as in certain cases one can see all the stages from black, yellow, light yellow and white leukodermic-like.

2. Black Pinta, Including the Bronzine and the Blue Varieties: Under this heading, too, several conditions apparently should be differentiated. (*a*) Patches of black or bronzine hyperpigmentation with occasionally a bluish tinge, not raised and not pruriginous are seen; fungi are not found microscopically, or only a few sporelike bodies on the surface of the epidermis; cultivation methods may show absence of fungi, or presence of penicillium-like, aspergillus-like and other molds identical with those which one finds at times on the skin of normal natives. The etiological rôle of these molds, so many species of which have been described by various observers, seems doubtful and as regards the cases seen by me in Honduras the organisms were in probability only saprophytes. These patches of hyperpigmentation appear similar to, or identical with, the various chloasmas (bronzine chloasma, etc.) that are observed in natives and Europeans all over the Tropics, and are probably not of direct mycotic origin. (*b*) Patches of hyperpigmentation are seen, associated with or following infections with fungi of the group *Trichophytoneae* (atrichophytons, epidermophytons, etc.). Some years ago I made the observation in Ceylon that chronic infections due to fungi of this group had in some cases a disturbing action on the pigmentation processes of the skin, which became either hyperpigmented or less pigmented, or apigmented, and that these patches of hyperpigmentation and hypopigmentation remained visible for years after the fungus had disappeared. The hyperpigmented patches in negroes are common in the inguinocrural region, also on the back and chest. (*c*) Black patches, caused by the presence of *Cladosporium mansoni* (tinea nigra) in large numbers, are seen.

3. White Pinta: Two conditions may be distinguished: (*a*) leukodermic patches, being the last stage in the process of depigmentation, which is represented first by the amycotic yellow patches, and apparently is not directly caused by any fungus; (*b*) depigmentation patches associated with or following chronic mycotic infections such as infections with the trichophytoneae and malassezia fungi.

ACCLADIOSIS

Historical.—The condition was first observed by me in Ceylon in 1907, but I did not fully describe it until 1916 in a paper in the *British Medical Journal.*

Fig. 39.—Acladiosis.

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It is caused by a peculiar fungus which I grew from the lesions. I sent cultures to Professor Pinoy of the Pasteur Institute. He described it botanically and called it after my name.

Geographic Distribution.—Cases have been observed in Ceylon, in the Federated Malay States, in Siam by Mendelson and in Macedonia by Lurie.

Etiology.—The condition is caused by a fungus, which, as stated, I first isolated from a case in Ceylon. Cultures were sent to Professor Pinoy, of the Pasteur Institute, who kindly investigated it botanically and classified it, giving it the name of *Accladium castellani* Pinoy, 1916. I will quote a portion of Professor Pinoy's description:

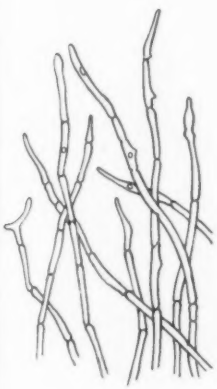

Figure 40

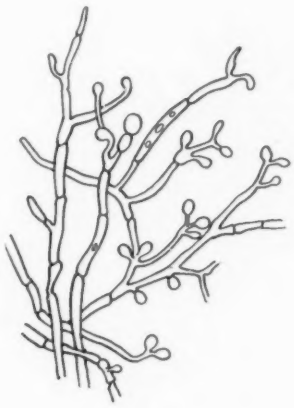

Figure 41

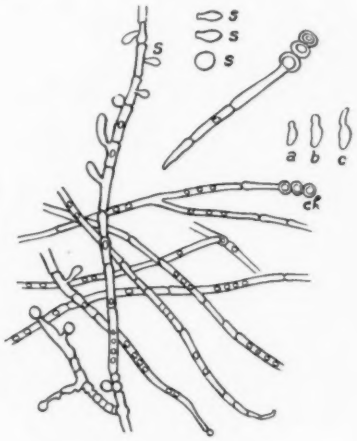

Figure 42

Fig. 40.—Accladiosis; microscopic appearance of the fungus in hanging drop culture, twenty-four hours old.

Fig. 41.—Microscopic appearance of the fungus in hanging drop culture, three days old.

Fig. 42.—Microscopic appearance of the fungus in hanging drop culture, five days old: *s*, pseudoconidia; *a*, *b*, *c*, development of hyphae from pseudoconidia; *ch*, chlamydospores.

The growth on artificial media (such as carrot, potato, glucose agar) consists of many small roundish masses, which later on may coalesce, covered by spiculated formations, giving them a prickly appearance, and consisting of erect, straight filaments, parallel to each other, or at times interlacing. These filaments are approximately 2 microns in diameter, and carry laterally pseudoconidia of variable shape, cylindriform, pyriform, or spherical, attenuated in size at their points of insertion. Most of these pseudoconidia are 4 microns in length with a breadth of 3 microns. This type of fructification recalls the type *Accladium* described by Bodin in certain species of the genus *Trichophyton* (Malmsten, 1848).

These pseudoconidia become detached and then develop by sprouting, and mycelial filaments are formed. Certain filaments produce spherical chlamydospores arranged in small strings, as found in certain fungi of the genus *Fusarium*. These small chains of chlamydospores are very frequently terminal, the dimensions being variable—8 to 10 microns (figs. 40, 41 and 42).

In cultures on carrot and potato the colonies are white, on dextrose agar often amber. Old cultures often show a certain amount of black pigmentation.

Microscopic Anatomy.—This investigation of the condition is far from being completed. From the preliminary investigation it would seem that the lesions are somewhat similar to those one sees in sporotrichosis, and that three types of lesions may be distinguished: (1) an epithelioid or tuberculoid type, with presence of giant cells; (2) a

Fig. 43.—Accladiosis (infection contracted in the tropics).

lymphoconnective tissue type (syphiloid); (3) a polymorphonuclear type (ecthymatous).

Clinical Symptoms.—In a well marked case ulcerative lesions are present all over the body, though they are in smaller number or absent altogether on the face, scalp, palms and soles. Most of the ulcers are sharply defined, roundish or oval, with red granulating fundus. In many cases there is abundant purulent secretion which collects and dries up in thick yellow crusts covering the ulcers. Gumma-like nodules and furuncle-like lesions may also be observed. The superficial lymphatic glands may be enlarged. The lesions in most cases give little pain, or none at all; itching is often completely absent, but occasionally the patient complains of slight pruritus. The general condition of the patient is not seriously affected for a long time. but he often complains of a certain degree of weakness and discomfort. Not infrequently

there is serotine fever. The blood has been examined in two cases in the Tropics, and in one case in the Balkanic zone: the Wassermann reactions were negative. In the first two cases the red blood corpuscles and hemoglobin content were slightly below the normal; in one there was eosinophilia (5 per cent) which may have been due to a concomitant *Ascaris lumbricoides* infection. In the Macedonian case, in which the blood was examined, there was a distinct leukocytosis (16,000 leuko-

Fig. 44.—Accladiosis in a Siamese man (from Dr. Mendelson).

cytes) of the polymorphonuclear type; in this patient there was abundant purulent secretion and serotine fever, which on some days reached 102 and 103 F.

Diagnosis.—A positive diagnosis can be made with certainty only by cultural methods. The microscopic examination alone is of little use, hyphomycetic elements being, as a rule, absent microscopically in the scrapings from the ulcers and contents of nodules. The material should

be inoculated in dextrose agar tubes. From four to eight days after inoculation small, yellowish, amber-colored colonies appear; they enlarge fairly rapidly, become hemispheric and often coalesce in a knotty mass. At times the colonies may not fuse together; each colony then remains separate, reaches a large size and occasionally presents peculiar radiating furrows as seen in certain species of trichophytons. In many cases in which the material has been collected from ulcerated lesions, the fungus grows in symbiosis with a coccus and it may be difficult to separate the two organisms. The malady is often taken for a syphilitic condition. The history, the negative examination of the lesions for spirochetes and the failure of mercury and arsphenamine treatment will exclude it. When the lesions are covered by raised, thick, bright, yellow crusts the condition must be differentiated from yaws: in accladiosis, on removal of the crusts, ulcers are found, while in yaws, the typical frambesiform nodules will be seen; in scrapings from yaws lesions *Spirochaeta pertenuis* will be found. Accladiosis can be differentiated from sporotrichosis and other diseases of hyphomycetic origin by cultural methods.

Prognosis.—The course of the disease may be long, and there is little or no tendency to spontaneous cure; but if a proper treatment is carried out a cure can be obtained fairly rapidly in the majority of cases. A few cases respond to treatment extremely slowly.

Treatment.—The treatment consists of giving potassium iodide in full doses (from 20 to 30 grains [1.3 to 2 Gm.] three times a day). The drug appears to act more rapidly at times if given in conjunction with a saltfree diet as suggested by Professor Pinoy. If the ordinary iodides are not well borne, sajodin and other similar preparations may be tried, but the result is not so satisfactory. Arsenic and mercury do not have any effect on the course of the malady. The ulcerated lesions should be kept clean by the use of a mercury perchloride lotion (1 in 2,000) or a weak lotion of compound solution of cresol.

LITERATURE

The current literature on fungi and fungous diseases is scattered but references can usually be found in the *Bulletin de l'Institut Pasteur* (Paris) and in the *Bulletin for Tropical Diseases* (London), while original papers are found in the principal medical journals, especially those on dermatology, bacteriology, pathology and parasitology. Some of the most important papers have appeared in the following journals: *Journal of the American Medical Association* (Chicago), *British Medical Journal* (London), *Lancet* (London), *Journal of Tropical Medicine and Hygiene* (London), *American Journal of Tropical Medicine* (Baltimore), *New Orleans Medical and Surgical Journal* (New Orleans), *Archives of Dermatology and Syphilology* (Chicago), *British Journal of Dermatology* (London), *Annales de l'Institut*

Pasteur (Paris), *Archives de Parasitologie* (Paris), *Annales de dermatologie et de syphiligraphie* (Paris), *Giornale italiano della malattie della pelle* (Milano), *Lo Sperimentale* (Florence), *Archiv für Dermatologie und Syphilis, Centralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten.*

In the annexed list some of the more important works of reference (books and monographs) are given.

WORKS OF REFERENCE (BOOKS AND MONOGRAPHS)

OLD PUBLICATIONS

Bonorden, H. F.: Handbuch der Allgemeinen Mykologie, Stuttgart, 1851.

Busse, O.: Die Hefen als Krankheitserreger, Berlin, 1897.

Eidam, E.: Mycologie, Berlin, 1872.

Fries: Systema Mycologicum, 3 vols., Gryphiswaldiae, 1821-1829.

Fuckel, L.: Symbolae Mycologicae Beitrage zur Kenntniss der rheinischen Pilze, Jahrbucher des Nassanischen Vereins fur Naturkunde, Weisbaden, 1869-1870. Continuation of foregoing, Weisbaden, 1872.

Kutzing, F. T.: Species Algarum, Lipsiae, 1849.

Micheli, P. A.: Nova Plantarum Genera, Florentiae, 1729.

Persoon, D. C. H.: Synopsis Methodica Fungorum, Gottingae, 1801.

Robin, Charles: Vegetaux Parasites, Paris, 1853.

RECENT PUBLICATIONS

Brumpt: Precis de Parasitologie, ed. 2, Paris, 1925, pp. 757-977.

Castellani, Aldo: Etiologie du Tokelau, Bull. Soc. de path. exot., 1923, no. 2.

Castellani, Aldo, and Chalmers, A. J.: Manual of Tropical Medicine, Chapters on Mycetes and Mycoses, New York, William Wood & Co., 1920.

De Beurmann and Gougerot: Les Sporotrichoses, Paris, 1912.

Grütze: Ueber variabilität pathogener Hautpilze, Centralbl. f. Bakteriol., 1926.

Guillermond: Les levures, Paris, 1912.

Guillermond and Tanner: The Yeasts, New York, 1920.

Kolk, Kraus and Uhlenhuth: Handbuch der pathogenen Microorganismen, Jena, 1926.

Pollacci and Nannizzi: I Miceti Patogeni, Sienau, 1923, 1924, 1925 and 1926.

Sabouraud: Les Teignes, Paris, 1910.

Saccardo: Sylloge fungorum, Padua, 1886 and 1906. Published in eighteen volumes, of which vol. iv., 1886, and vol. xviii., 1906, are the most useful, as they deal with the hyphomycetes. In the complete work 57,660 species of fungi are described.

Vuillemin: Les aleuriosporés, Nancy, 1911.

Wehmer: Die Pilzgattung Aspergillus, Geneve, 1911.

Winter, Rehm, Fischer, and Lindau: Die Pilze Deutschlands, Oesterreichs und der Schweiz, Leipzig, 1881 to the present. This is from Rabenhorst's "Kryptogamen-Flora," vol. i, chapter viii, 1907, and contains Hyphomycetes (erste Halfte), Mucedinaceae and Dematiaceae by Lindau.

COLLOIDAL GOLD

A METHOD FOR THE PREPARATION OF COLLOIDAL GOLD FOR THE LANGE TEST ON CEREBROSPINAL FLUID *

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NEW YORK

While there is considerable disagreement between investigators as to the exact value of the various observations with Lange's colloidal gold test for cerebrospinal fluid,[1] all are unanimous in their opinion regarding its value as a useful confirmatory test in the diagnosis and the differentiation of syphilitic and nonsyphilitic diseases of the central nervous system.

The test is based on the observations of Zsigmondy [2] that proteins will protect various colloidal substances from being precipitated by electrolytes. The degree of protection has been found to be specific for each protein, and is expressed in terms of milligrams of the protein that is capable of protecting 5 cc. of colloidal gold against 0.5 cc. of a 10 per cent solution of sodium chloride.

It has been known for a long time that the protein content in spinal fluid varies in pathologic conditions of the central nervous system. Accordingly, Lange took advantage of Zsigmondy's observations and endeavored to apply them to the quantitative determination of protein in the spinal fluid; however, contrary to his expectation, he found that an excess of protein precipitated colloidal gold instead of protecting it.

The exact nature of the reaction is not well understood: Lange regarded it as due to the proteins of the spinal fluid; Jaeger and Goldstein [3] considered it a purely physical reaction of an electrolytic nature; while Zaloziecki [4] believed it to be an immunity reaction. Whatever the nature of the reaction may be, its usefulness in the diagnosis of certain diseases is well established.

While the technic of the test is simple, it has one great obstacle; and that is the preparation of suitable colloidal gold sol. This is extremely difficult, in spite of the fact that gold lends itself easily to transformation into a colloidal state by a great many organic and inorganic substances. The great difficulty encountered in preparing col-

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* From the Biochemical Department of Lebanon Hospital Laboratory, New York.

1. Lange: Ztschr. f. Chemotherap. **1**:44, 1912; Berl. klin. Wchnschr. **51**:97, 1912.
2. Zsigmondy: Ztschr. f. anal. Chem. **40**:697, 1901.
3. Jaeger and Goldstein: Ztschr. f. d. ges. Neurol. u. Psychiat. **16**:391, 1913.
4. Zaloziecki: Deutsche Ztschr. f. Nervenh. **41**:73, 1913.

loidal gold is due to the fact that the slightest variations in the technic of preparation produce gold sols of different physical properties, such as: color, hydrogen-ion concentration, degree of dispersity and concentration of the disperse phase, surface tension, viscosity, electric conductivity, etc. Any of these properties will change the gold's behavior toward biologic substances. In order that a gold sol could be used in the Lange test its properties must be so adjusted that it should fulfil the following requirements: [5]

1. It must be transparent and of a brillant red orange or salmon red color.

2. Five cubic centimeters must be completely precipitated in one hour by 1.7 cc. of a 1 per cent solution of sodium chloride.

3. It must be neutral in reaction.

4. It must give a typical paretic curve with a known paretic fluid, and must not produce a greater reaction than one with normal spinal fluid in the first tube.

There are a great number of methods recorded in the literature for the preparation of colloidal gold of various colors. Historically, it dates from the days of the alchemists. The first comprehensive work on this subject, however, was published in 1857 by Faraday,[6] who prepared gold sols by reducing gold salts with phosphorus in ether. The greatest advancement in this field was made by Zsigmondy,[7] who reduced faintly alkaline solutions of gold chloride with formaldehyde. He worked out the conditions necessary for obtaining a uniform highly disperse gold sol, which was at once stable and sensitive to reagents.

To give some idea as to the number and variety of substances that can be used to prepare gold sols, I shall mention but a few: Donau [8] reduced gold salts with carbon monoxide. Blake [9] used acetylene as a reducing agent. Gutbier and Hofmeier [10] prepared gold solutions of varying colors by reducing gold salts with hydrazine, hydrazine hydrate and phenyl hydrazine. Vanino [11] and Eicke [12] used carbohydrates. Von Veimarn [13] used glycerol. Bredig,[14] Svedberg,[15] and Manheims and Bernhard [16] used electrical dispersion methods.

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5. Kolmer: Infection, Immunity and Specific Therapy, ed. 2, Philadelphia, W. B. Saunders Company, 1920, p. 557.
6. Faraday: Proc. Roy. Soc. London, Phil. Tr. **147**:145, 1857.
7. Zsigmondy: Ann. der Chemie **301**:29, 1898.
8. Donau: Monatsch. f. Chemie **26**:525, 1905.
9. Blake: Am. J. M. Sc. **4**:381, 1903.
10. Gutbier and Hofmeier: Ztschr. f. anorganisch Chemie **45**:77, 1905.
11. Vanino: Kolloid.-Ztschr. **11**:51, 1907.
12. Eicke: München. med. Wchnschr. **60**:2713, 1913.
13. Von Veimarn: Kolloid.-Ztschr. **39**:166, 1926.
14. Bredig: Ztschr. f. Elektrochem. **4**:51, 1908.
15. Svedberg: Kolloid.-Ztschr. **1**:229, 1907.
16. Manheims and Bernhard: J. Lab. & Clin. Med. **11**:235, 1925.

Colloidal gold to be used for spinal fluids is most generally prepared by the method of Miller, Brush, Hammers and Felton,[17] who use the Zsigmondy technic of reducing alkaline gold chloride with formaldehyde. The technic is elaborate, as all glassware must be chemically clean, the water must be triply distilled, and all reagents must be of the highest purity. Even when the most exacting precautions are taken, however, it is not always possible to obtain a workable gold sol.

In my endeavor to devise a simple and easily reproducible method for preparing a colloidal gold suitable for the Lange test on spinal fluid, I tried out a number of different methods and studied the conditions necessary to produce a sol of the desired properties; I tried to find a method which would not be too exacting in its demand as to the purity of the reagents and water. Such conditions I was gratified in finding by making use of the observation of Vanino [11] that saccharose (ordinary table sugar) was a good reducing agent for gold chloride. Vanino used the following technic: He placed in a flask 1 cc. of gold chloride (0.003176 Gm. gold), 100 cc. of doubly distilled sterile water and 10 cc. of a 1 per cent solution of saccharose, and kept it in the dark for a few days, when a blue color developed. He further found that heat hastened the development of the color, and that the addition of alkali produced a red color. Since saccharose is not ordinarily a reducing agent, Vanino believes that its reducing power is due to the glucuronic acid into which the sugar is hydrolyzed by the hydrochloric acid of the gold chloride solution. He also states that ordinary distilled water cannot be used, as it already contains some substances to reduce the sugar.

I am rather inclined to doubt the correctness of the last two statements. That the hydrogen chloride molecule present in the gold chloride is not the factor responsible for the reduction of the sugar is evident from the fact that when the gold chloride is neutralized with sodium hydroxide before the sugar is added, the reduction of the gold chloride is much more efficient than when the solution is acid. The saccharose is probably hydrolyzed into dextrose and levulose. That dextrose is a good reducing agent for gold has been shown by Eicke.[12] This I can confirm from personal experience. I have also found levulose to be a good reducing agent for gold chloride. At the beginning, probably, a small fraction of the saccharose is hydrolyzed into dextrose and levulose, and the products of the hydrolysis immediately reduce a few particles of gold chloride to colloidal gold; these, in turn, act as a catalytic agent to hasten the hydrolysis of the rest of the saccharose. The catalytic action of colloidal metals is well known, and they are often referred to as the "inorganic ferments."

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17. Miller, Brush, Hammers and Felton: Bull. Johns Hopkins Hosp. **26**:391, 1915.

As to the reducing substances present in ordinary distilled water, it hardly seems possible that the small amount of impurity present should interfere with the reduction of the gold chloride by destroying the saccharose, since the amount of sugar used by Eicke is much in excess of the required amount. In practically all the methods for preparation of colloidal gold, attention is called to the necessity of using doubly or triply distilled water; the reason given is the sensitivity of colloids to electrolytes. When one considers, however, that, as is the case with colloidal gold used in the Lange test, it is not precipitated by so large an amount as 0.4 per cent of sodium chloride, it does not seem reasonable to assume that incomparably smaller amounts of electrolytes should have such detrimental effects. The fact that electrolytes are added during the process of preparation also throws doubt on the general assumption that slight amounts of electrolytes in the water are responsible for unsuccessful gold preparations.

By using saccharose as the reducing agent, I prepared hundreds of samples of red gold sols with ordinary distilled water. The most favorable concentration of saccharose was found to be 0.1 per cent. Gold chloride is added to the sugar solution, which is then brought to a boil; a weak alkali solution is added slowly while the solution is boiling. When a small amount of alkali is added, the solution first turns light violet-blue; but it keeps on getting darker and darker with the progressive additions of alkali until at the end, with the addition of a few drops, there is a sudden sharp change from dark violet-blue to a beautiful brilliant red. This procedure, while giving favorable results, has its drawback in that one has to start adding the alkali when the proper temperature is reached. If one begins to add the alkali too early, somewhat cloudy solutions are obtained; if one begins too late, some reduction and formation of blue gold will have taken place, and the final product will be too violet.

The reaction of colloidal gold solutions is of the greatest importance and is the primary cause of unsuitable solutions. Sodium hydroxide has a protective action on the gold particles and makes them more resistant to the action of electrolytes, while hydrogen chloride has the opposite effect. This is demonstrated by the following experiment: A gold sol was prepared, 5 cc. of which was completely precipitated by 1.7 cc. of 1 per cent sodium chloride in one hour, and was unaffected by 1 cc. of a 0.4 per cent solution of sodium chloride. This gold sol was distributed in a dozen test tubes, 5 cc. to each tube. To six tubes were added varying amounts of hundredth normal hydrogen chloride, and to the other six tubes were added varying amounts of hundredth normal sodium hydroxide. All of the tubes containing the acid showed

varying degrees of reduction, depending on the amount of acid present, while none of the alkali tubes showed any reduction, as is shown in table 1.

The same experiment was repeated, but in addition to the acid and alkali, 1 per cent sodium chloride was added to each tube. As is shown in table 2 the acid tubes were completely reduced in one hour by minute amounts of sodium chloride, while much greater amounts were required to produce slight reduction in the alkali tubes.

TABLE 1.—*Reduction of Gold Sols by the Use of Varying Amounts of Acid and Alkali*

	Acid						Alkali					
Tube	1	2	3	4	5	6	7	8	9	10	11	12
Number of cubic centimeters of hundredth normal hydrochloric acid	0.2	0.4	0.6	0.8	1.0	2.0	...	...	...	...	...	...
Number of cubic centimeters of hundredth normal sodium hydroxide	...	...	...	...	...	...	0.2	0.4	0.6	0.8	1.0	2.0
Reduction after 1 hour*	0	0	1	2	2	4	0	0	0	0	0	0

* 0 indicates no change in color; 1, red blue; 2, purple; 3, blue; 4, pale blue, and 5, complete reduction.

TABLE 2.—*Reduction of Gold Solutions by the Use of Varying Amounts of Acid and Alkali with the Addition of Sodium Chloride*

	Acid						Alkali					
Tube	1	2	3	4	5	6	7	8	9	10	11	12
Number of cubic centimeters of hundredth normal hydrochloric acid	0.2	0.4	0.6	0.8	1.0	2.0	...	...	...	...	...	...
Number of cubic centimeters of hundredth normal sodium hydroxide	...	...	...	...	...	...	0.2	0.4	0.6	0.8	1.0	2.0
Number of cubic centimeters of 1% sodium chloride	0.1	0.1	0.1	0.1	0.1	0.1	1.0	1.0	1.0	1.0	1.0	1.0
Reduction in 1 hour	0	1	3	4	5	5	2	1	1	0	0	0

The protection afforded by alkalis to colloidal gold sols against precipitation by electrolytes is only comparatively so, and thus, when a great excess of alkali is added to colloidal gold, the alkali will precipitate the gold. When the gold solution is red, the neutrality of the solution could be adjusted by adding acid or alkali, provided the reaction is near the neutral point or faintly alkaline. When the gold solution has a slight violet tinge, showing that some precipitation of gold particles has already been accomplished, the solution will most likely be somewhat acid in reaction, and addition of alkali to adjust the reaction will prove valueless. A solution like this should be discarded.

It is obvious, then, that it is safer to have the reaction of the medium somewhat alkaline during the process of preparation of colloidal gold. This can easily be accomplished by using the proper indicator to adjust the reaction of the solution in the beginning of the process. I found that cresol phthalein answered this purpose in a satisfactory manner.

Most textbooks recommend that the final adjustment of the reaction of colloidal gold solutions be done with alizarine red. This indicator is not satisfactory, however, because of the difficulty in noting the change in color. Novick [18] advocated a more accurate method by titration with twentieth normal solutions of sodium hydroxide or hydrogen chloride. That amount of acid or alkali is added, as the case may be, which will produce complete precipitation of 5 cc. of colloidal gold with 1.7 cc. of a 1 per cent solution of sodium chloride. I found, however, that in adjusting colloidal gold sols for the Lange test, it is not so much the degree of reduction of the gold by electrolytes that should be sought as, what is of greater importance, the degree of protection against precipitation by electrolytes; that is, that 5 cc. of colloidal gold should not be affected by 1 cc. of a 0.4 per cent solution of sodium chloride.

The following method for the preparation and titration of colloidal gold is satisfactory, and I was able to prepare dozens of samples of gold without a single failure.

METHOD FOR PREPARATION OF COLLOIDAL GOLD

Clean the glassware by boiling for half an hour in a solution of ivory soap; wash well with tap water and then soak for a few hours in warm chromic acid cleaning solution. This solution is prepared as follows:

Potassium dichromate	80 Gm.
Concentrated sulphuric acid	120 cc.
Water	1000 cc.

Wash well with tap water and lastly with distilled water and dry in a hot oven.

Prepare cresol phthalein indicator paper by immersing strips of fat-free, ashless filter paper into a 1 per cent alcoholic solution of cresol phthalein (1 Gm. of cresol phthalein in 100 cc. of 95 per cent alcohol), and dry at room temperature.

In a large clean beaker place 1,000 cc. of ordinary distilled water and 10 cc. of a 1 per cent solution of gold chloride in water. Add 1 Gm. of saccharose (cane sugar) and dissolve by mixing with a glass stirring rod. Add slowly, drop by drop, tenth-normal sodium hydroxide, mixing the contents all the while. From time to time, take out one drop of the solution on the end of the stirring rod and place on a piece of the cresol phthalein indicator paper; when the end point is reached, the spot of the paper touched by the solution turns pink. A good pink color should be obtained, which should not fade in thirty seconds. It takes about 5 cc. of the sodium hydroxide solution to produce the proper reaction. Place the

18. Novick: Correction of Colloidal Gold Solutions as Applied to Lange Reaction; Simple and Accurate Titration Method, Arch. Neurol. & Psychiat. **15**:471 (April) 1926.

beaker over a bunsen flame and heat; before the boiling point is reached a faint color will develop, and when the solution begins to boil a beautiful clear salmon red gold sol will be obtained. Boil until no more color develops. It is better to boil it a little too long rather than not long enough. When cool, titrate the solution as follows:

Into each of three test tubes place 5 cc. of colloidal gold and add to the first tube 0.4 cc. of a 1 per cent solution of sodium chloride; to the second tube add 1.7 cc. of 1 per cent solution of sodium chloride; the third tube serves as a control. Let it stand for one hour at room temperature and follow one of the two following procedures:

If the first tube remains unchanged and the second tube is not completely reduced, the solution is too alkaline and, accordingly, not sensitive enough. Set up seven tubes containing 5 cc. of the colloidal gold each, and titrate as shown in table 3.

The tube containing the least amount of acid which remained unchanged is taken as correct, and the amount of acid to be added is calculated from this.

If the first tube in the preliminary titration shows a slight reduction and the second tube is completely reduced, the gold sol is slightly too acid and, hence, too sensitive. Set up seven tubes as indicated in the first procedure but add the corresponding amounts of hundredth-normal sodium hydroxide instead of the acid.

TABLE 3.—*Titration of Colloidal Gold*

Tube	1	2	3	4	5	6	7 (control)
Number of cubic centimeters of colloidal gold	5	5	5	5	5	5	5
Number of cubic centimeters of hundredth normal hydrochloric acid	0.1	0.2	0.3	0.4	0.5	0.6	None
Number of cubic centimeters of 1 per cent sodium chloride	0.4	0.4	0.4	0.4	0.4	0.4	0.4

A number of colloidal gold solutions prepared by this method were tested on known paretic, syphilitic and normal spinal fluids, and were checked by a colloidal gold sol prepared with triply distilled water by the formaldehyde process. Good agreements were obtained, and in no instance was a reaction obtained with normal spinal fluids.

SUMMARY

1. Saccharose was found to be a good reducing agent for the preparation of colloidal gold.

2. Alkalis have a stabilizing effect on colloidal gold, protecting it against the precipitating action of electrolytes.

3. Acids have the opposite effect, making colloidal gold more sensitive to the precipitating action of electrolytes.

4. A method is described whereby a colloidal gold sol can be easily prepared with ordinary distilled water by reducing an alkaline solution of gold chloride with saccharose.

5. A method is described for the titration of colloidal gold to make it adaptable for the performance of the Lange test on cerebrospinal fluids.

CLINICAL STUDIES ON THE KAHN REACTION

IV. SPECIFICITY OF REACTION IN FEBRILE DISEASES *

JUI-WU MU, M.D.
AND
HARTHER L. KEIM, M.D.
PEKING, CHINA

Specificity is the most important of all requirements of any diagnostic procedure. A serologic reaction for syphilis is not an exception to this rule, and the importance of its specificity in the presence of nonsyphilitic pathologic conditions cannot be overemphasized.

The specificity of the Wassermann reaction has long been studied, and it was early learned that false positive reactions were obtained in a great variety of nonsyphilitic conditions, especially in the febrile diseases. As the technic of the complement-fixation reaction was improved, fewer false positive tests were obtained. For example, it is claimed that the modified Wassermann reaction as proposed by Kolmer possesses a high degree of specificity. Kolmer and Steinfield,[1] after examining the reaction with a regard to its specificity, believe that it does not yield false positive results; they are of the opinion that positive tests occurring without clinical or historical evidence of syphilis indicate latent syphilis and demand careful study of the patients concerned.

Since Kahn proposed his flocculation test, in 1922, numerous favorable reports have appeared with regard to the sensitivity and specificity of this test. A composite summary of the more than 170 articles which have thus far appeared would indicate that as workers become more informed on the correct technic of the test, their observations are more favorable. It is well to recall at this point that practically all comparative studies on this test with the Wassermann test are made by workers who are masters of the technic of the Wassermann test, but who are beginners with the Kahn test.

Few of these reports [2] include any study on the specificity of the Kahn reaction in febrile diseases. In view of this fact, it was felt desirable to make this study with the hope of ascertaining whether febrile diseases, particularly those which run a more or less sustained

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* From the Division of Dermatology and Syphilology of the Department of Medicine, Peking Union Medical College, Peking.

1. Kolmer, J. A., and Steinfield, E.: J. Lab. & Clin. Med. **10**:1, 1924.

2. Keim, H. L., and Kahn, R. L.: J. Lab. & Clin. Med. **10**:1013, 1925. Kilduffe, R. A.: Am. J. Syph. **9**:318, 1925. Hartman, F. W., and Reyner, C. E.: Kolmer Complement Fixation as Specific Test for Syphilis, J. A. M. A. **82**:196 (Jan. 19) 1924.

course, produce any change in the colloidal properties of the blood which may lead to false positive Kahn reactions.

The data herein presented are based on the study of 124 consecutive serums from 106 patients admitted to the medical service of the Peking Union Medical College during the past year. These include thirty-five

TABLE 1.—*Analysis of Cases of Positive or Doubtful Serologic Reactions with Fever*

Diagnosis	Total No. of Cases Studied	Cases Showing Positive or Doubtful Reactions: Serial Number	Wassermann Reaction*	Kahn Reaction*	Temperature (Centigrade)	
Typhus fever.....	35	1	3, 3, 3, —, —	1, 2, 3	39.8	(103.6 F.)
			2, 1, ±, —, —	1, 1, 2	35.5	(97.7)
		2	4, 4, 4, —, —	1, 4, 4	40	(104)
			4, 4, 4, —, —	±, 1, 1	26.6	(97.9)
		3	±, —, —, —, —	—, —, —	39.5	(103.1)
			—, —, —, —, —	—, —, —	37	(98.6)
		4	—, —, —, —, —	—, ±, ±	39.6	(103.1)
			—, —, —, —, —	—, —, —	37.2	(99)
		5	±, ±, ±, —, —	—, —, ±	40	(104)
			—, —, —, —, —	—, —, —	37	(98.6)
		6	±, —, —, —, —	—, —, —	39.6	(103.3)
			—, —, —, —, —	—, —, —	37.4	(99.3)
		7	1, ±, —, —, —	—, 1, 3	40	(104)
			3, 2, 2, —, —	—, 1, 2	37.4	(99.3)
		8	2, 2, 2, 2, ±	—, —, 2	39.2	(102.6)
			4, 3, 2, —, —	1, 4, 4	37	(98.6)
		9	4, 4, 2, —, —	4, 4, 4	39	(102.2)
			4, 4, —, —, —	2, 3, 3	37.1	(98.8)
Relapsing fever.....	25	10	2, 2, 1, —, —	—, 1, 2	40.4	(104.7)
			2, 2, —, —, —	—, 1, 2	37.2	(99)
		11	±, —, —, —, —	—, —, —	40.4	(104.7)
			2, —, —, —, —	—, ±, 1	36.8	(98.2)
		12	2, —, —, —, —	—, ±, ±	40	(104)
			1, 1, —, —, —	—, —, 1	37.2	(99)
		13	3, 3, 2, —, —	—, 2, 3	40.4	(104.7)
			4, 4, 3, —, —	—, 4, 4	37.2	(99)
Pneumonia.....	21	14	4, 4, 4, 4, 3	4, 4, 4	39.8	(103.6)
			4, 4, 4, 4, 4	3, 4, 4	37	(98.6)
		15	4, —, —, —, —	—, —, 4	41.2	(106.2)
			4, 2, —, —, —	—, 2, 3	37.2	(99)
		16	4, 4, 4, —, —	4, 4, 4	40	(104)
			4, 4, 4, 4, ±	—, 4, 4	37	(98.6)
		17	4, 4, 3, —, —	2, 2, 2	39	(102.2)
			4, 4, 4, 1, —	1, 3, 3	36.9	(98.4)
		18	4, 4, ±, —, —	2, 2, 2	39	(102.2)
			1, —, —, —, —	2, 2, 2	37	(98.6)
Typhoid fever.....	25	..	All negative	All negative		
Total number of cases.....	106					

* The upper line shows the reactions of the serum taken during fever on the day indicated in table 2. The lower line shows the reactions after the subsidence of fever.

cases of typhus fever, twenty-five of relapsing fever, twenty-one of pneumonia and twenty-five of typhoid fever. Each specimen of blood was taken at or above the temperature of 39 C. (102.2 F.), and repeated when the temperature was approximately normal. The serums were examined with the Kahn reaction and for comparison were tested also

with the Kolmer-Wassermann test. The technic used for the latter is exactly as described by Kolmer.[3] The precipitation technic employed is that described by Kahn in 1925.[4]

On analyzing tables 1 and 2, one is immediately impressed with the remarkable concordance of the results of the two tests, complete agreement occurring in 56 per cent and relative agreement in 44 per cent. There was not a single case in which one test was frankly negative while the other was strongly positive. Among the eighteen patients whose serums gave positive reactions, only six (serial numbers 3, 4, 5, 6, 10 and 15) did not have any historical or clinical evidence of syphilis.

TABLE 2.—*Evidence of Syphilis in the Cases of Positive Serologic Reactions*

Diagnosis	Serial Number	Blood Tested on: Day of Illness	Blood Tested on: Day After Subsidence of Fever	Evidence of Syphilis
Typhus fever.....	1	13	7	History of exposure and penile sore; scar in right groin
	2	7	6	History of exposure and gonorrhea
	3	15	13	No historical or clinical evidence
	4	9	5	No historical or clinical evidence
	5	9	8	No historical or clinical evidence
	6	8	12	No historical or clinical evidence
	7	10	10	History of exposure
	8	13	9	History of exposure; penile scar and urethral discharge
	9	8	10	History of exposure
Relapsing fever.....	10	5	8	No historical or clinical evidence
	11	2	7	History of penile sore; penile scar and enlarged inguinal glands
	12	3	6	History of exposure; penile scar
	13	6	5	History of exposure; inguinal glands enlarged and scar in left groin
Pneumonia.....	14	4	6	History of exposure and gonorrhea
	15	3	10	No historical or clinical evidence
	16	4	7	History of exposure and penile sore; penile scar and venereal warts
	17	10	20	History of exposure and bubo; scars in groins and enlarged inguinal glands
	18	2	9	History of exposure and penile sore
Typhoid fever.....	..	..	..	None had any historical or clinical evidence

In four of these patients, the serologic reactions were exceedingly doubtful during the febrile period, and on repetition during their convalescence were found to be negative. The other two (serial numbers 10 and 15) had repeatedly positive serologic reactions and will have to be accepted as having syphilis without clinically discoverable signs or symptoms.

A comparison of the results of the Kahn reaction at various temperatures as well as a similar comparison with the results obtained with the Kolmer-Wassermann reaction reveals the fact that in this study the

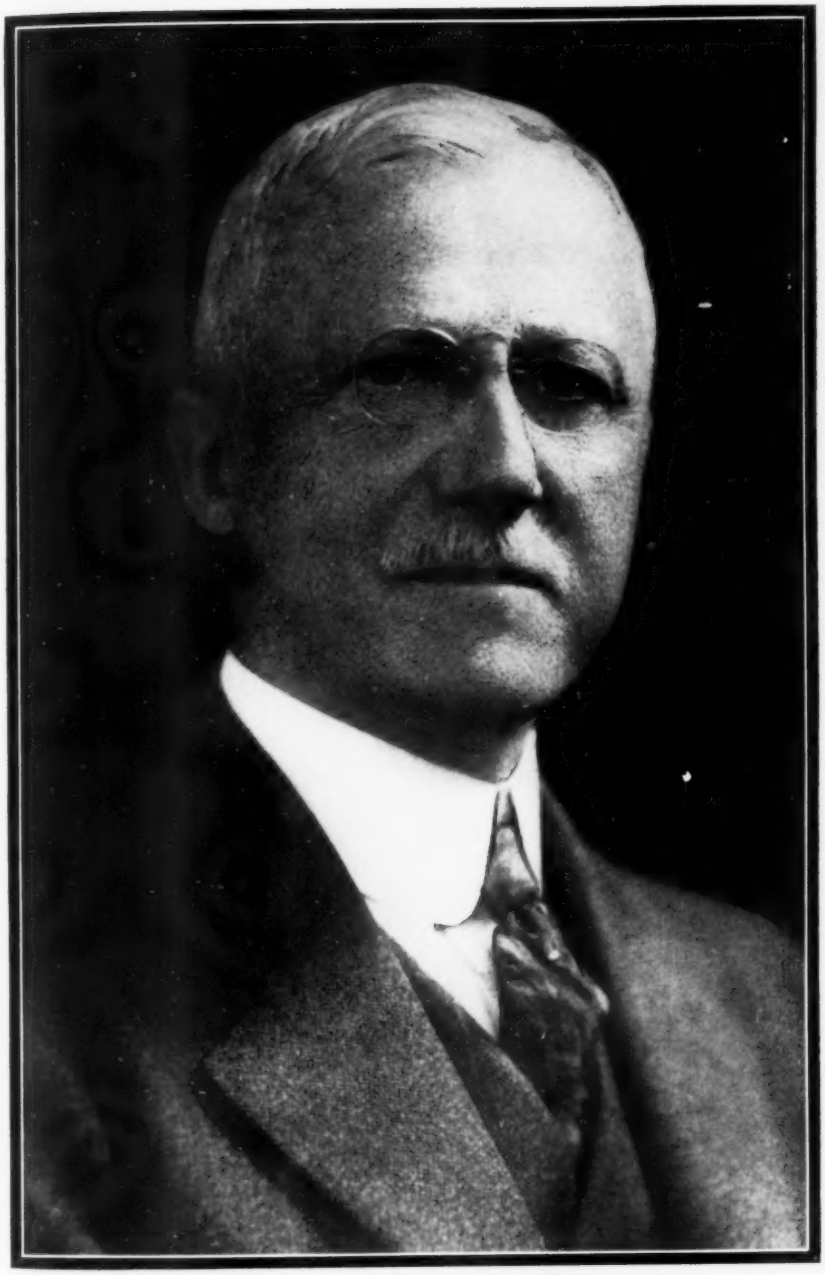
3. Kolmer, J. A.: Am. J. Syph. **6**:74, 1922.

4. Kahn, R. L.: Serum Diagnosis of Syphilis by Precipitation: Governing Principles, Procedure and Clinical Application of the Kahn Precipitation Test. Baltimore, Williams & Wilkins Company, 1925.

former reaction has a definite tendency toward positivity at lower temperatures. From this observation, it would appear that the positivity of the Kahn reaction is definitely not increased by the febrile condition.

SUMMARY

The blood of 106 febrile patients—including patients with pneumonia and typhus, relapsing and typhoid fever—was examined with the Kahn and with the Kolmer-Wassermann reactions. The examinations were made at the height of the fever and repeated in from five to twenty days after the subsidence of the fever. Both reactions gave parallel and specific results. The balance was somewhat in favor of the Kahn reaction, since its results fluctuated least as a result of the fever.



THOMAS CASPAR GILCHRIST, M.D.
1862-1927

Obituaries

THOMAS CASPAR GILCHRIST, M.D.
1862-1927

American dermatologists were shocked to learn of the death of Dr. Gilchrist at Johns Hopkins Hospital on Nov. 14, 1927, from cirrhosis of the liver. He had not been in his usual robust health for several months, and he did not receive the usual benefit from his vacation abroad. The nature and the seriousness of his condition, however, did not become manifest until his acute illness, which ended fatally in two weeks.

Thomas Caspar Gilchrist, the son of Robert and Emma Gilchrist, was born, June 15, 1862, at Crewe, Cheshire, England. His early education was received at Fairfield Academy, Manchester. From 1882 to 1888 he studied at Owens College, Victoria University, Manchester. He became M.R.C.S., L.S.A. (England) in 1899, and received the honorary M.D. degree from the University of Maryland in 1907. He was president of the American Dermatological Association in 1909; honorary member of the Italian Dermatological Society; corresponding member of the Berlin Dermatological Society and a member of the Dermatological Section of the British Medical Association, of which he was vice president in 1902.

He was a member of the Maryland Club, University Club, Baltimore Country Club, Baltimore Whist Club, Churchman's Club and the Florestan Club.

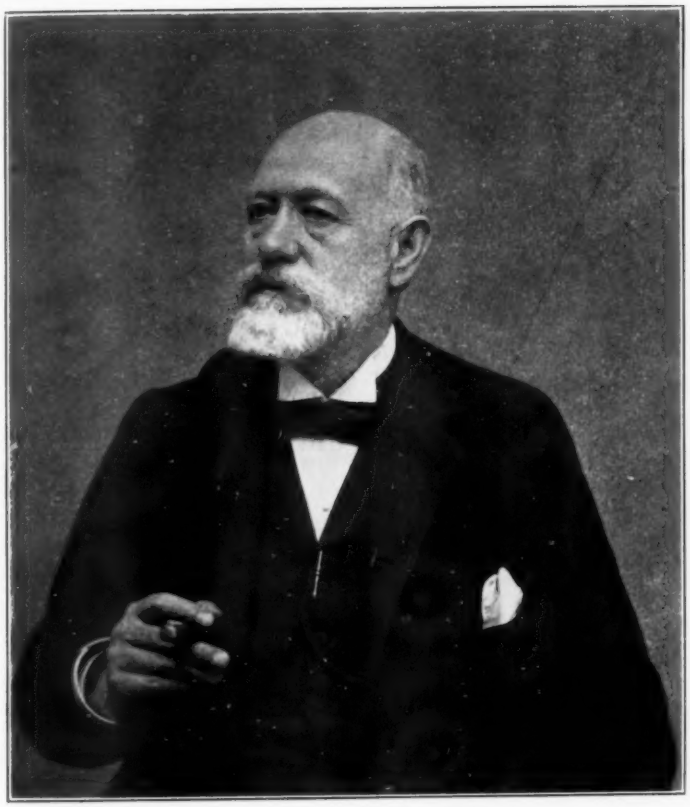
Dr. Gilchrist came to this country in October, 1889. After a time spent with Dr. Duhring, in Philadelphia, he began the practice of medicine in Baltimore in 1890. He became associated with Dr. Morrison at the Johns Hopkins Hospital, and after Dr. Morrison's death became the chief of the dermatologic department of the dispensary. He was made clinical professor of dermatology in the Johns Hopkins University School of Medicine in 1897, and held that title until his death. He was also professor of dermatology at the University of Maryland.

In his early association at Johns Hopkins his energy and application to work were enormous, and many contributions to dermatologic literature were published. The most important were those concerning blastomycetic infections of the skin. The work was a classic, and it was not only original, but complete. At this time he did much microscopic work in Dr. Welch's laboratory, and his artistic ability enabled him to make many valuable drawings, some of which are used for illustrations in present day textbooks. He gave careful consideration

to every point of view before coming to any definite conclusions about conditions of the skin. He gave close attention to any advance in dermatologic treatment, and was one of the pioneers in radium and roentgen-ray therapeutics.

Dr. Gilchrist was a friendly, companionable person. He delighted in his home life, and his hospitality was unbounding. On the occasions when he had the opportunity to entertain his colleagues, whether in small groups or in such bodies as the American Dermatological Association, he was an ideal host—genial, solicitous and generous.

He will be missed, particularly at the meetings of dermatologic societies, where his serious and intense participation in discussions was supplemented by his jokes, his humorous criticisms and his friendly personalities. His death is a loss that will be felt in the field of dermatology.



SAMUEL SHERWELL, M.D.
1841—1927

SAMUEL SHERWELL, M.D.
1841—1927

Dr. Samuel Sherwell, emeritus professor of dermatology at the Long Island College Hospital, died at his home in Brooklyn, Dec. 20, 1927, in his eighty-sixth year. His sister, Mrs. Florence Rice, with whom he lived, survives him.

Dr. Sherwell was born in 1841 in Dartmoor, England, of a family of culture, and was one of nine children.

His youth was spent amid the trying circumstances of the political upheavals of that period in Europe, and he was deeply impressed with the important events and people of the time. It was also the golden age of literature of the Victorian period, and, as he was an omnivorous reader, he spent many a happy hour with the works of Thackeray, Macaulay, Dickens and others.

The *New York Tribune* of Horace Greeley came to him regularly from his uncle in America, to stimulate his imagination and to teach him the wonderful resources and opportunities of the country to which his family had already decided to send him when he grew to manhood.

After his school days were over he started in London as an assistant to the publisher of the *Shipping and Mercantile Gazette*, a paper since merged into *Lloyd's Register*. He was there but a short time when his uncle Augustus Graham sent for him to come to America. Mr. Graham had settled in Brooklyn, and had become one of its prominent citizens, being the founder of the Brooklyn Institute of Arts and Sciences. Through Mr. Graham's influence Sherwell became a passenger on the U. S. Frigate *Niagara* which was to lay the first transatlantic cable. After a most exciting and interesting voyage he arrived in New York on Aug. 9, 1858.

When his uncle died, in 1861, he made an extensive tour of the western states and a leisurely journey into the Rocky Mountain region where he did much big game hunting and had many interesting adventures. Returning just as oil discoveries in western Pennsylvania threw the whole country into feverish excitement, he rushed to the center of interest. Fortune did not smile on him in his oil ventures, so on the advice of Dr. S. S. Porter of Franklin, Pa., he decided to study medicine.

He entered the University of Michigan in 1866, and completed his studies at the University and Bellevue Medical College, New York, in 1868. He was an intern at the Brooklyn Hospital in 1869.

After finishing his internship, Dr. Sherwell completed his medical education in Vienna, studying dermatology under the great Hebra and

laryngology under Schrotter. Here he became an intimate friend of George Henry Fox, Edward B. Bronson, L. D. Bulkley and A. R. Robinson, all of whom later became noted dermatologists in New York.

After the close of the clinics Dr. Sherwell made an extensive tour of Austria, Italy and Switzerland, returning just at the outbreak of the Franco-Prussian war. He was persuaded by Dr. Marion Sims and Sir William McCormack who headed the Anglo American Ambulance Corps to join them. He served through the war, as surgeon, with the rank of major and received the military order "pour la Merite" from the Bavarian government.

In 1871 he returned to New York and commenced practice in the Heights section of Brooklyn, and remained active until the time of his death.

In the earlier days he did a great deal of work in laryngology, being one of the pioneers in this branch of medicine; but later he specialized entirely in dermatology, in which field he was also a pioneer.

Dr. Sherwell's first appointment was surgeon to the Department of Skin and Throat Diseases at the Brooklyn Eye and Ear Hospital in 1872. In 1877 he was appointed lecturer on diseases of the skin at the Long Island College Hospital, and later he became the first professor of this branch of medicine.

He served the Long Island College Hospital actively for about thirty years and at the time of his death was emeritus professor and consulting dermatologist to this hospital and to most of the other large hospitals of Brooklyn.

Professor Sherwell was twice president of the New York Dermatological Society and once president of the American Dermatological Association.

He contributed many monographs on his special subject and reported and described the first case of pellagra in this country.

His method of removing epitheliomas by curettage and cautery is the equal of any practiced today.

In 1915, at the age of 75, Dr. Sherwell went to France and offered his services to the Red Cross, but at this early stage of the Great War his services could not be accepted. He returned to Brooklyn in 1917 and served as a consultant on the advisory staff during the war.

Sherwell was a picturesque figure. The enumeration of his many activities gives only an intimation of the variety and adventures of his career. Consider the outstanding events: Participation in the laying of the first cable between America and Europe—the first deep-sea cable; across the plains of America before there was a railroad; in the oil fields of Pennsylvania in the days of the early excitement; active service throughout the Franco-Prussian War. Hardly any man participated in

more of the outstanding events of the middle of the nineteenth century. He has given entertaining descriptions of this part of his career in his memoirs, which can be recommended as instructive and interesting reading.

For many years he was one of the prominent men in American dermatology. He was a regular attendant at the meetings of the American Dermatological Association, where his frank, breezy, humorous personality made him interesting and welcome, and where his broad knowledge of dermatology and his sound sense made him an instructive and respected member. He was one of the last of the pioneers in American dermatology.

He was a genial, kindly, warm-hearted man, and he left a host of friends who admired and loved him.

News and Comment

New Hospital in Philadelphia.—An institution to be known as the Skin and Cancer Hospital of Philadelphia has recently been organized, with Edgar B. Moore as president. Mr. Moore is president of the Penn Worsted Mills and a director of the Benjamin Moore and Company paint manufacturers of New York.

A building located at 806-808 Pine Street, Philadelphia, has been purchased to house this institution. After it has been remodeled and renovated, the institution will be in full running order for the reception and treatment of all classes of conditions of the skin.

The building will also be equipped with laboratories for research work, especially for the investigation of the well known resistant and chronic forms of diseases of the skin and cancer.

A board of directors composed of representative residents of Philadelphia has entered into the work with enthusiasm, and Dr. Albert Strickler is medical director.

Eighth International Congress in Dermatology and Syphilis.—A letter from Prof. Carl Rasch of Copenhagen, who has been selected by his Danish colleagues to be president of their society, makes the following announcement which will be of interest to all American dermatologists:

"It has now been finally decided that the Eighth International Congress of Dermatology and Syphilology is to be held at Copenhagen in August, 1930, and we are gladly looking forward to a big participation of American dermatologists."

Abstracts from Current Literature

Clinical Results with Ephedrine Therapy. T. L. Althausen and I. C. Schumacher, Arch. Int. Med. **40**:851 (Dec.) 1927.

Ephedrine was tried in one case of toxic erythema and spectacular recovery occurred. In seven cases of urticaria, the benefit from ephedrine therapy was doubtful in two, and absent in five. Three patients with angioneurotic edema failed to improve.

Untoward effects, such as nausea, insomnia and palpitation, were encountered in 30 per cent of the patients treated. Red blood cells and casts were found in the urine of a few patients following ephedrine therapy. A few patients have acquired a tolerance to the drug.

Rattner, Chicago.

Hypoglycemia in Scleroderma: The Metabolism in Eight Cases with Reference to the Function of Glands of Internal Secretion. W. T. Longcope, J. A. M. A. **90**:1 (Jan. 7) 1928.

Longcope reviews previous studies on the etiology of scleroderma. These have indicated the probability of endocrinous disturbance, particularly of the thyroid, as an etiologic factor in the disease.

The author records in detail a case of the generalized form in which the unusual features were the extreme bronzing of the skin, the asthenia, the relatively low blood pressure, the low basal metabolism rate, the low fasting blood sugar and finally the attacks of vertigo, restlessness, confusion and delirium following short periods of fasting and accompanied by hypoglycemia as pronounced as occurs in reactions to insulin. During these attacks there were no apparent alterations in the acid-base balance or the organic phosphates of the blood. The blood sugar curve was somewhat lower than the average normal. In five other cases of the generalized form the blood sugar and other chemical constituents of the blood were normal. In three cases the basal metabolic rate was subnormal. In a fatal case atrophy of one suprarenal gland and interstitial orchitis were found.

As a result of these observations, the author believes that disturbances in the function of the glands of internal secretion, which occasionally accompany scleroderma, may occur, in some instances, as a result of the involvement of these organs by the generalized process, and thus may not have any direct bearing on the etiology of the disease.

The Treatment of Tineal Dermatitis of the Extremities. W. A. Pusey, J. A. M. A. **90**:27 (Jan. 7) 1928.

For the acute outbreaks, Pusey thinks that dilute aluminum subacetate solution is superior to any other wet dressing. Even in the acute stage it is desirable to paint a stronger antiseptic between the toes. Metaphen, potassium permanganate, and mercurochrome-220 soluble are suggested for this purpose. When the acute stage has subsided, potassium permanganate soaks combined with Whitfield's ointment are recommended. For the chronic interdigital types, mechanical removal of the thickened epidermis and applications of tincture of iodine or Whitfield's ointment are beneficial. Roentgenotherapy is generally regarded as useful.

Cutaneous Roentgen-Ray and Radium Therapy. G. M. MacKee, J. A. M. A. **90**:28 (Jan. 7) 1928.

This article is one of a series being published by the Council on Physical Therapy of the American Medical Association. In condensed form the author presents the well known indications and limitations of these energies.

TATTOOING AND METHOD FOR ITS REMOVAL. M. D. SHIE, J. A. M. A. **90**:94 (Jan. 14) 1926.

Shie presents a short discussion of the ethnologic aspects of tattooing and gives a résumé of the methods of producing and removing this embellishment. He then records his experience with the method of Variot for removal of the marks. This consists in tattooing into the design a 50 per cent solution of tannic acid followed by rubbing the area with a silver nitrate pencil. The resulting eschar is allowed to separate spontaneously. The author has had excellent results by this method.

MICHAEL, Houston, Texas.

EXFOLIATIVE DERMATITIS. H. D. HALDIN-DAVIS, Brit. J. Dermat. **39**:435 (Nov.) 1927.

The historical aspect of exfoliative dermatitis is first discussed in this paper, and the following classification is presented: (1) the classic disease around which Hebra and Wilson fought; (2) a well known recurrent form mild in type; (3) the dermatitis exfoliativa of infants, often called Ritter's disease, and (4) the exfoliative dermatitis following the administration of organic compounds of arsenic. The occurrence of a lymphocytosis in many cases is mentioned and emphasized. The pathologic processes of this disease are discussed in detail, with references to the literature and the author's cases. Seven photomicrographs accompany the article. The microscopic study demonstrates, among other things, that all parts of the skin are almost equally affected, but Haldin-Davis is inclined to believe that it begins in the deeper parts, and that the injury to the horny layer and the consequent exfoliation is caused by the constant welling-up of the inflammatory products from below. The preponderance of lymphocytes as the infiltrating cell in one section prompted the conclusion that possibly the infiltrating cells always consist chiefly of cells of the same character that predominate in the blood stream, the blood in this case showing 70 per cent lymphocytes. The relationship of exfoliative dermatitis to other dermatoses is discussed. Its kinship to tuberculosis, as a tuberculid, with reference to the case described by Bruusgard as erythroderma exfoliative universalis tuberculosa and that of Fiocca as "erythrodermia maligna tuberculosa," is discussed. The writer feels that when tuberculosis does occur in this condition it is merely a terminal infection. The relationship to various blood diseases is considered, lymphatic or myeloid leukemia, and lymphosarcoma and lymphadenoma. In this connection, he is of the opinion that a possible connection exists between exfoliative dermatitis and the leukemias, and thinks that detailed pathologic investigation of cases will probably bring to light cases of a transitional type bridging the gap between those cases of leukemia which do not present cutaneous signs, and those of exfoliative dermatitis in which changes in the blood are absent, or perhaps only present from time to time.

EXFOLIATIVE DERMATITIS. G. H. LANCASHIRE, Brit. J. Dermat. **39**:446 (Nov.) 1927.

During the last ten years, forty-two cases of this disease have been observed of a total of 94,000 new cases at the Salford Hospital for Skin Disease. The majority of these cases have been secondary. Men and women were equally affected. The age at which it occurred in men was between 50 and 60; and the greater number of women affected were below 30 years of age. Two case histories are briefly presented. Sugar tolerance tests in two cases revealed identical abnormalities; namely, blood sugar — fasting level, 118 per cent; after dextrose, forty-five minutes, 181 per cent; after ninety minutes, 182 per cent. A third case, of Savatard's, also showed abnormality in sugar tolerance. In discussing etiology, Lancashire mentions that the blood sugar changes should probably be placed among the effects rather than the causes. The etiology is still a matter of theory and he mentions briefly the

factor of toxemia exerting its effects on the vasomotor centers; sensitization to some chemical substance as pointed out by Cranston Low in those cases following metallic poisoning; that those cases following psoriasis and seborrheic dermatitis may be due to sensitization to the organisms which probably cause these conditions, and that in primary cases the antigen may come from a bowel infection. In some instances, focal infection may be the cause.

PEMPHIGUS: THE USE OF WHOLE BLOOD TRANSFUSION AS AN AID IN THERAPY. PRELIMINARY REPORT. L. HOLLANDER, Brit. J. Dermat. **39**:450 (Nov.) 1927.

Reports of six cases of pemphigus vulgaris are presented, in which treatment with whole matched blood was used. In five of the cases there was great improvement in the general and skin condition, and in the sixth case although improvement was noted in the skin condition death occurred from an intercurrent acute infection. Hollander feels that the results shown from the effect of transfusion of whole blood make it worthy of further investigation on a larger scope, and suggests the possible advantageous use of blood transfusion in other serious dermatologic conditions, such as exfoliative dermatitis. The following procedure for transfusion of blood in pemphigus is described: The patient's blood is typed into one of four groups, and one or more donors of the corresponding types is selected. Direct transfusion of from 500 to 600 cc. of blood is carried out in weekly intervals and repeated from three to six times. The preparation of the patient is similar to that in the intravenous administration of arsphenamine. He states that ordinarily the reactions produced by the transfusion of whole blood are negligible and mentions the reactions that may occur during the administration of the whole blood, such as, tingling of the toes and fingers, numbness of the extremities, palpitation, air hunger and signs of appearing cyanosis, for which he discontinues the transfusion and gives 10 minims of 1 to 1,000 epinephrine hydrochloride intradermally while the patient is still on the table.

WIEN, Chicago.

PROGNOSIS OF SYPHILIS IN THE LIGHT OF MODERN METHODS OF TREATMENT. L. W. HARRISON, Brit. J. Vener. Dis. **3**:299, 1927.

The author believes that the prognosis today is considerably more favorable than it was before the use of neoarsphenamine. Before this treatment was employed cure in the sense of eradication was effected in only a negligible proportion of the cases; now, with the adequate treatment of patients with seronegative primary lesions, one may expect between 95 and 100 per cent cure. In the stage of secondary manifestations, within six months of infection, 75 per cent of the patients are cured.

Incidences of recurrences of neurosyphilis, palsy of the cranial nerve and visceral involvement have been considerably reduced since the adoption of mixed treatment, and the outlook in the worst event, that is, the onset of general paralysis, has been improved greatly by malarial treatment.

THE PROPHYLAXIS OF NEUROSYPHILIS. REDVERS IRONSIDE, Brit. J. Vener. Dis. **3**:273, 1927.

This is a brief, clear discussion of the present knowledge of syphilis with especial emphasis on involvement of the central nervous system. The author states that 30 per cent of all patients with syphilis show early changes in the spinal fluid, with a corresponding increase in the percentage during the stage of secondary manifestations, and the so-called latent period. The various observations on the spinal fluid are discussed as to their relative values, the increase in cell count being of most importance.

Prophylaxis depends on effective sterilization of the patient, if possible before generalization of the infection has occurred. Thorough physical exam-

ination and a study of the spinal fluid are recommended even in the primary stage. During the latent stage, the author pleads for complete physical, neurologic and serologic examination, biennially for ten or fifteen years. Alcoholism is a distinct factor in neurosyphilis. Marriage should not be contemplated until the patient has had at least three years of active treatment, and two years of symptomless observation, with repeated negative reactions on the blood and cerebrospinal fluid following the first six months of treatment.

As to prophylaxis regarding children, contraception is advised when there is knowledge of previous syphilis in parents. Pregnancy in infected mothers should not be interfered with, but antisyphilitic treatment should be forced. A child of syphilitic parents should not pass the third year without serologic examination which should be repeated in the seventh year.

H. RATTNER, Chicago.

TWO CASES OF FOLLICULITIS ULERYTHEMATOSA RETICULATA (MACKEE AND PAROUNAGIAN) COMBINED WITH LICHEN SPINULOSUS, EPIDERMAL CYSTS, AND FOLLICULITIS DECALVANS. H. W. BARBAR, Proc. Roy. Soc. Med. **20**:176 (Dec.) 1927.

Two patients — a brother and sister — were of exceptional interest because in both were combined conditions which have been separately described and which have excited considerable discussion as to their significance and relationships. On the cheeks and temples in both patients was seen the peculiar follicular pitting described by MacKee and Parounagian *(J. Cutan. Dis.* **36**:339, 1918) as "folliculitis ulerythematosa reticulata." In both, but particularly in the sister, were large numbers of epidermic cysts exactly similar to those seen in histologic sections from MacKee and Parounagian's patients. In these cases some of the cysts were as large as a large pea, whereas in MacKee and Parounagian's patients they were apparently microscopic. On the limbs and trunk were follicular horny plugs, which varied in appearance and degree from those seen in ordinary keratosis pilaris to the filiform spines of so-called lichen spinulosus. In certain situations on the limbs and trunk, there was follicular atrophy which resulted in deep pits. On the scalps of both patients, there was cicatricial atrophy with the production of bald areas on the vertex. It will thus be seen that in this brother and sister were follicular lesions involving practically all parts of the body in which pilosebaceous follicles exist (the palms and adjacent part of the anterior surface of the wrist were entirely free); these lesions comprised horny plugging, lichen spinulosus, formation of epidermic cyst, atrophy with pitting, and bald areas on the scalp. The cases thus bring into line the follicular atrophy of the face described by MacKee and Parounagian, and the syndrome described by Graham Little, Dore, Wallace Beatty and Speares and others of lichen spinulosus and folliculitis decalvans.

POROKERATOSIS: ITS CAUSATION AND TREATMENT. HUGH W. ACTON, Indian J. M. Research **15**:349 (Oct.) 1927.

Porokeratosis, although a distinct clinical entity, is merely a form of hyperkeratosis. It is characterized clinically by the occurrence of raised cornlike lesions, which as they enlarge form an irregular, raised wall, which surrounds an atrophic depressed center. Histologically, it is characterized by an increased vascularity of the papillary vessels which causes acanthosis and hyperkeratosis. With the continued vascularity the endothelial cells and fibroblasts multiply in the corium and constrict the vessels by pressure; atrophy sets in, causing the depressed depigmented wrinkled center. The association of a familial tendency and the lowered basal metabolic rate suggests that there is a partial correlation with hypofunction of the thyroid gland. The correlation is not complete, as these lesions are not found in other conditions of hypofunction of the thyroid such as myxedema and cretinism. The lesions can be cured

in two or three weeks with proper thyroid medication. Porokeratosis is therefore a localized keratosis with central atrophy (morphea) and falls into the large group of so-called skin diseases, xeroderma, scleroderma, keratosis follicularis and morphea, which are all partially associated with hypofunction of the thyroid.

These conclusions were the result of investigation in eight cases.

GUY, Pittsburgh.

THE FRONTIERS OF LICHEN PLANUS. ITS RELATIONS WITH PSORIASIS AND PARAPSORIASIS. L. BROCQ, Bull. Soc. franç. de dermat. et syph. **34**:507, 1927.

In this short note on certain clinical manifestations of lichen planus, Brocq calls attention to atypical forms of the disease, which on the one hand, may simulate psoriasis, and on the other, cutaneous atrophies. He cites a case of lichen planus in which the condition had been diagnosed as psoriasis by competent dermatologists; only the most careful examination revealed the true nature of the case. The debut of lichen planus as an erythematosquamous eruption is not sufficiently stressed in most texts. A second case is described in which the diagnosis of lichen planus or parapsoriasis en plaques was most difficult. As to the latter disease, while en gouttes and en plaques forms are reasonably well defined, Brocq is not yet certain of the nosographic position of the lichenoid type. The latter has as many, if not more, affinities with lichen planus as with parapsoriasis.

LICHEN PLANUS IN INFANCY. M. G. PETGES, Bull. Soc. franç. de dermat. et syph. **34**:515, 1927.

In some 5,600 cases of diseases of the skin in children, Petges has encountered 10 cases of lichen planus. The youngest child in this series was 6½ months old. Study of these cases added nothing to the present knowledge of the pathogenicity of the disorder. In children, lichen planus seems to occur oftener than in adults in the acute form and to run a shorter course.

A CASE OF LICHEN PLANUS STRIATUS OF RADCLIFFE CROCKER. J. M. PEYRI, Bull. Soc. franç. de dermat. et syph. **34**:517, 1927.

In a boy, aged 3, a papular eruption developed on the back of the right hand, with subsequent development of similar lesions in a linear arrangement on the arm. The case corresponded to that described by Crocker as lichen planus striatus.

PATHOLOGY OF LICHEN PLANUS. R. SABOURAUD, Bull. Soc. franç. de dermat. et syph. **34**:521, 1927.

Sabouraud calls attention to certain histologic features of lichen planus. The primary site of the lesions is in the papillary body. Essentially, it consists of an infiltration of mononuclear cells. This infiltration distends the papillae and constitutes a subepidermic node which produces the papule characteristic of the disease. The epidermis is secondarily involved. Rarely, giant cells are found in the infiltration. The microscopic observations do not indicate whether the disease is of endogenous or exogenous origin.

THE PRESENCE OF NERVE FIBRILS AND LESIONS OF NERVE TISSUE IN THE PAPULE OF LICHEN PLANUS. L. M. PAUTRIER and DISS, Bull. Soc. franç. de dermat. et syph. **34**:522, 1927.

Utilizing newer histologic methods, the authors have studied the finer elements of nerve tissue in this disease. Their observations are described in such detail as to preclude satisfactory exposition in a short abstract. In the

main, however, they have noted a proliferation of nerve radicals, but they are not yet satisfied about the origin of these new nerve elements. The increase in nerve fibers occurs at all stages of papule development.

MELANIN PIGMENTATION IN LICHEN PLANUS. G. LEVY, Bull. Soc. franç de dermat. et syph. **34**:534, 1927.

Clinically, pigmentation is one of the features of lichen planus. The pigment is melanin. Pathologically, melanoblasts are absent at the site of the lesion, but increased at its periphery; while chromatophores are more prominent in the dermal infiltration.

LICHEN PLANUS. JEANSELME and BURNIER, Bull. Soc. franç. de dermat. et syph. **34**:538, 1927.

In 100 cases of the disease, these observers have noted 46 in which the eruption was strictly on cutaneous sites, 32 with combined cutaneous and buccal involvement and 22 in which the lesions were limited to the buccal mucosa. They saw one case in a child under 1 year of age. They have obtained better results with neoarsphenamine than with sodium cacodylate. In a small series of patients treated with irradiation of the paravertebral regions (Gouin's method), amelioration or cure resulted in about 50 per cent of the cases.

CLINICAL NOTES ON ONE HUNDRED AND EIGHT CASES OF LICHEN PLANUS. HUDELO and RABUT, Bull. Soc. franç. de dermat. et syph. **34**:540, 1927.

In this series the disease predominated in adults. Nervous stress or neuroticism seemed to be a factor in the development of the disease. The authors have given up the use of metallic arsenic (sodium arsenate) in favor of neoarsphenamine. They found radiotherapy of the sympathetic system valuable.

ACTION OF ARSENIC IN LICHEN PLANUS. CARLE, Bull. Soc. franç. de dermat. et syph. **34**:543, 1927.

Carle has abandoned metallic salts of arsenic in this disease. Even in doses large enough to produce toxic effects the results are inconstant. With organic arsenic preparations he has obtained occasional success. Recently, the patients in two cases have responded promptly to bismuth. Carle believes that lichen planus often develops on a syphilitic terrain, and under these conditions, arsenical preparations produce the prompt cures that one occasionally encounters.

THE TREATMENT OF LICHEN PLANUS BY INJECTIONS OF SODIUM BROMIDE. K. HÜBSCHMANN, Bull. Soc. franç. de dermat. et syph. **34**:558, 1927.

Four patients with the disease were treated by intravenous injections of a 10 per cent solution of sodium bromide in physiologic sodium chloride. Lebedjev has shown that this treatment has a decidedly beneficial influence on many pruriginous dermatoses. All four patients responded promptly with rapid amelioration of the pruritus and a slower involution of the eruption.

A CASE OF LICHEN PLANUS OF NINE YEARS' DURATION TREATED BY SPINAL IRRADIATION AND INTRAVENOUS INJECTIONS OF SODIUM THIOSULPHATE. J. WATRIN, Bull. Soc. franç. de dermat. et syph. **34**:563, 1927.

Treatment with organic arsenicals did not have any effect. The patient was then given one irradiation over the vertebral column without response, but the condition cleared up after ten injections of sodium thiosulphate, which were administered because a moderate acidosis was discovered.

LUMBAR PUNCTURE IN LICHEN PLANUS. P. RAVAUT, Bull. Soc. franç. de dermat. et syph. **34**:567, 1927.

Ravaut says that lumbar puncture has a definite antipruritic effect particularly in lichen planus. He has seen a single puncture cure the disease. In rebellious cases three, or even four, withdrawals of spinal fluid at intervals of from eight to ten days were necessary. This procedure, however, is reserved for the most severe cases. He removes from 6 to 8 cc. of fluid.

RESULTS OBTAINED BY LUMBAR PUNCTURE AND CONDITION OF THE SPINAL FLUID IN LICHEN PLANUS. L. M. PAUTRIER, Bull. Soc. franç. de dermat. et syph. **34**:571, 1927.

In seven cases following lumbar puncture transitory amelioration of the pruritus was noted in all. There was no definite effect on the eruption. The spinal fluid was normal in all cases.

TREATMENT OF LICHEN PLANUS BY RADIOTHERAPY. J. GOUIN and A. BIENVENUE, Bull. Soc. franç. de dermat. et syph. **34**:573, 1927.

In this paper, the authors consider only their method which is irradiation over the vertebral column. They employ unfiltered roentgen-ray treatment with the tube placed over the fourth dorsal spine, and in some cases (localization of the disease on the legs) an accessory field centering over the twelfth dorsal spine. The dose is 5 Holzknecht units. They believe that the ray produces effects on the neurovegetative system, but not on the spinal cord itself. The method has been used since 1919 with good results. Pruritus is rapidly relieved in many cases; the objective manifestations of the disease disappear in the majority of cases in from one to three weeks. In lichen planus of the mucous membranes, filtered irradiation (from 1 to 2 mm. aluminum) is employed.

RESULTS OF TREATMENT OF PATIENTS WITH LICHEN PLANUS BY IRRADIATION OF THE VERTEBRAL REGION. DO THESE RESULTS PERMIT PATHOGENIC DEDUCTIONS? LOUSTE, LEVY, FRANCKEL and JUSTER, Bull. Soc. franç. de dermat. et syph. **34**:591, 1927.

The authors employed both filtered and unfiltered radiation. With the former, there were thirty-two cures and eight failures; with the latter, ten successes and eight failures. Some of the patients required only one treatment; many, however, were given three or four seances at intervals of one month. Though this method of treatment gives definite results in lichen planus, the authors do not believe that it permits plausible deductions concerning the pathogenicity of the disorder.

INDIRECT RADIOTHERAPY OF LICHEN PLANUS. K. GAWALOWSKI, Bull. Soc. franç. de dermat. et syph. **34**:594, 1927.

Though radiation of the spine gives favorable results in lichen planus, it is impossible to say whether the effects are due to an action on the cord itself, the spinal ganglions or the parasympathetic fibers. In an effort to elucidate this obscure question, the author submitted several patients who had lichen planus to roentgen-ray radiation of the axilla and the anterior surface of the thigh (over the region of the large vascular trunks).

The response was comparable to that obtained by vertebral radiation, and it was, therefore, concluded that each of these methods produce their effects on sympathetic fibers. This effect may be akin to that obtained by periarterial sympathectomy or, perhaps, to an unknown action on autonomic fibers.

TREATMENT OF FOUR CASES OF LICHEN PLANUS BY THE METHOD OF GOUIN. LAURENT, Bull. Soc. franç. de dermat. et syph. **34**:597, 1927.

Gouin's method consists of unfiltered roentgenization over the vertebral column. In the four patients thus treated there was one cure, two ameliorations and one failure.

REFLECTIONS ON RADIOTHERAPY IN LICHEN PLANUS. J. PAYENNEVILLE and BILLIARD, Bull. Soc. franç. de dermat. et syph. **34**:598, 1927.

These authors have treated six patients with the disease by irradiation of the vertebral column; two by Gouin's technic (unfiltered) and four by Pautrier's (filtration and cross-firing). They conclude from this experience that this form of treatment is the most efficacious known at present. Its most pronounced effect is on the pruritus. They favor Pautrier's method.

THE TREATMENT OF LICHEN PLANUS BY RADIATION OF EXTENSIVE SKIN SURFACES. J. G. PRIETO, Bull. Soc. franç. de dermat. et syph. **34**:599, 1927.

The author believed that the explanations given for the favorable response of patients with lichen planus to roentgenization of the spinal region were not entirely satisfactory. In particular, the effect might be due to an action on the skin itself, not explainable, but, nevertheless, present. He therefore irradiated a large abdominal area in five cases of lichen planus and, obtaining favorable results, concluded that the roentgen ray acts exclusively on the skin irrespective of the region irradiated.

THE TREATMENT OF PATIENTS WITH LICHEN PLANUS BY SPINAL RADIOTHERAPY. L. M. PAUTRIER, Bull. Soc. franç. de dermat. et syph. **34**:602, 1927.

Pautrier gives his reasons for the conception and employment of this method, reasons which are admittedly purely conjectural. The dose used by him is 4 Holzknecht units, filtered through 5 mm. aluminum and cross-fired. The region irradiated is from the first dorsal to the fifth lumbar vertebra. By this means he has treated thirty-five patients and has obtained cures in two thirds of the cases. Amelioration of the itching was rapid. In nine cases, a second dose, from three to six weeks after the first, was necessary. In seven cases of lichen planus in the buccal region, three of the patients were cured, and one was improved; the treatment failed in three cases. In only one case in the series was there a recurrence. There were no unfavorable effects. Pautrier does not believe that the action of the rays can be explained by a therapeutic skin effect, as maintained by Prieto. He failed to corroborate that observer's results.

THE EXTERNAL TREATMENT OF LICHEN PLANUS. CARLE, Bull. Soc. franç. de dermat. et syph. **34**:611, 1927.

Carle recommends the vegetable tars, particularly oil of cade as the best external application in this disease. He uses it in an ointment in combination with camphor and balsam of peru.

TREATMENT OF LICHEN PLANUS BY INJECTIONS OF URIAGE WATER. CHAUCHARD, Bull. Soc. franç. de dermat. et syph. **34**:615, 1927.

A case is reported in which intravenous injections of this mineral water lead to a cure in about three months.

FAILURE TO INOCULATE LICHEN PLANUS IN MAN AFTER TWENTY-ONE ATTEMPTS. L. M. PAUTRIER, Bull. Soc. franç. de dermat. et syph. **34**:618, 1927.

Material was obtained from three cases and injected intradermally and rubbed into a scarified area. In twenty-one subjects there was failure to produce the disease. While this result does not completely exclude the microbic origin of the disease, it speaks strongly against this hypothesis.

LICHEN PLANUS PRODUCED BY EMOTIONAL STRESS. G. PETGES, Bull. Soc. franç. de dermat. et syph. **34**:627, 1927.

In Petges' experience emotional stress has never produced lichen planus. The emotional strains encountered are an effect, rather than the cause, of the disease.

LICHEN PLANUS PRIMARILY PRODUCED BY PROLIFERATION AND LESIONS OF NERVE TISSUE AT SITE OF PAPULE. L. M. PAUTRIER and A. DISS, Bull. Soc. franç. de dermat. et syph. **34**:631, 1927.

These authors repeat the observations presented in a previous article on their investigations of the nerve elements in lichen planus. They found proliferation of the nerve fibrils preceding any other pathologic change. This proliferation and certain pathologic changes in the nerve radicals are present during stages of development of the papules. So far they have not had an opportunity to investigate the regressive stages of the papules. Pautrier and Diss were unable to determine definitely the origin of the newly formed nerve fibrils or to ascertain whether the changes were of peripheral or central origin.

THE PATHOGENESIS OF LICHEN PLANUS. E. RAMEL, Bull. Soc. franç. de dermat. et syph. **34**:635, 1927.

A general discussion of the more recent hypotheses regarding the etiology of the disease is presented. Ramel believes disorders of the vegetative nervous system play a definite rôle in the genesis of lichen planus.

THE ETIOLOGY OF LICHEN PLANUS. F. KOGOJ, Bull. Soc. franç. de dermat. et syph. **34**:638, 1927.

Kogoj discusses in considerable detail the diathetic, microbic and nervous hypotheses of the etiology of lichen planus. The author is an adherent of another hypothesis which in substance is as follows. Lichen planus (and acuminatus) is a dermatosis provoked by an unknown virus exercising its pathologic faculties in a special soil, the hyperkeratotic diathesis. It is most probable that this diathesis is based on an endocrinous dysfunction, which in turn is subordinated to or associated with a congenital or acquired functional abnormality of the autonomic nervous system.

THE PATHOGENICITY OF LICHEN PLANUS. F. SAMBERGER, Bull. Soc. franç. de dermat. et syph. **34**:652, 1927.

Samberger has enunciated a theory of psoriasis; namely, that it is caused by staphylococci acting on a skin which reacts in a special way. This particular reactivity has been designated the parakeratotic diathesis. In analogy with this conception, there is another hypothetical diathesis; the hyperkeratotic, and this type produces the objective lesions of lichen planus. For example, a case is cited of sensitivity to primrose in which lichen planus papules arose on the areas rubbed with primrose leaves. According to Samberger, in the majority of cases lichen planus is eczema which has been transformed into lichen planus by the presence of the hyperkeratotic diathesis.

LICHEN NITIDUS AND LICHEN PLANUS. A. CIVATTE, Bull. Soc. franç. de dermat. et syph. **34**:666, 1927.

Civatte is of the opinion that lichen nitidus is a rare form of lichen planus. The supposition of its tuberculous origin can be dismissed. In support of his point of view, the author discusses the case of a patient whom he saw in 1911, the results of which he has not published clinically. There was a generalized eruption composed of lesions of both lichen planus and lichen nitidus with some elements that could be interpreted as transitional forms. Biopsies taken

from different regions showed typical lichen planus and lichen nitidus histologically. One section (illustrated) revealed an anatomic papule of lichen planus and lichen nitidus in juxtapostion. Civatte does not think that this instance is one of the coexistence of the two diseases; he interprets the case as evidence of their unity.

LICHEN CORNÉ AND LICHEN PLANUS. NICOLAS, J. GATÉ and G. MASSIA, Bull. Soc. franç. de dermat. et syph. **34**:675, 1927.

The authors discuss the relationship between lichen planus and lichen corneus hypertrophicus. Some authors regard the latter as an atypical lichen planus; others, notably Pautrier, as a form of abnormal lichenification. A case is described in detail in which clinically lichen planus, lichen obtusus corneus and lichen corneus hypertrophicus were present. Pautrier has insisted that the latter condition is always preceded by pruritus, but this train of circumstances has not been constant in the author's experience. For them, lichen corneus hypertrophicus is not a lichenification in the signification of that term, but an atypical form of lichen planus.

LICHEN CORNEUS HYPERTROPHICUS IS AN ABNORMAL FORM OF LICHENIFICATION WHICH MAY BE SUPERIMPOSED UPON LICHEN PLANUS OR BE COMPLETELY INDEPENDENT OF IT. L. M. PAUTRIER, Bull. Soc. franç. de dermat. et syph. **34**:684, 1927.

The author's point of view that lichen corneus hypertrophicus is an atypical form of lichenification is briefly discussed. He has seen fifteen cases of that disease in recent years; in seven it coexisted with lichen planus, and in eight lichen planus was absent. On clinical and histologic grounds, Pautrier believes that lichen planus and lichen corneus hypertrophicus are independent disorders; the latter is a verrucous form of lichenification.

THE PATHOLOGIC ANATOMY OF SOME HYBRIDS OF LICHEN PLANUS AND LICHENIFICATION. L. M. PAUTRIER and A. DISS, Bull. Soc. franç. de dermat. et syph. **34**:688, 1927.

The article contains a histologic study of the mixed forms of lichen planus and lichen corneus hypertrophicus. Pathologically, the former presents a characteristic histologic structure; none of its features are found in the latter disease. In the borderline and mixed cases, superimposed lichenification explains the clinical features as well as the persistence of the hybrid lesions after radiotherapeutic cure (by spinal irradiation) of the lesions of lichen planus.

LICHEN SPINULOSUS FOLLOWING ACUTE LICHEN PLANUS. LORTAT-JACOB and LEGRAIN, Bull. Soc. franç. de dermat. et syph. **34**:692, 1927.

A case is reported in which lichen planus was followed by lichen spinulosus. The authors regard the latter disorder as a syndrome (a cutaneous reaction) which may be consecutive to various cutaneous conditions, among them lichen planus not infrequently.

AN UNDESCRIBED PIGMENTED PAPILLOMATOSUS. GOUGEROT and CARTEAUD, Bull. Soc. franç. de dermat. et syph. **34**:719, 1927.

The patient was a woman, aged 21, who first noticed the disorder in 1921. It began on the upper part of the abdomen and spread slowly at first, but in May, 1927, it suddenly became generalized. It was most marked on the trunk. The elementary lesion was a small, flat, rugous papule: at first it was pink, and later, brown. Confluence lead to the formation of patches, which at a distance resembled pityriasis versicolor.

TUBERCULOUS ULCERATION OF THE LIP. LORTAT-JACOB and POUMEAU-DELILLE, Bull. Soc. franç. de dermat. et syph. **34**:723, 1927.

A report of a case of ulceration of the mucous surface of the lower lip which was complicated by a severe stomatitis is given. Tubercle bacilli were found in sections from the ulcer. The patient had active pulmonary tuberculosis.

A CASE OF ZONIFORM SYPHILIDS. LORTAT-JACOB and POUMEAU-DELILLE, Bull. Soc. franç. de dermat. et syph. **34**:723, 1927.

The zosteriform arrangement of the patches and local adenopathy were the features of this case of early secondary syphilis.

BILATERAL FACIAL PARALYSIS OCCURRING DURING TREATMENT WITH ARSPHENAMINE IN A PATIENT WHO SIX WEEKS PREVIOUSLY HAD A CHANCRE OF THE CHIN. HUDELO and BARBE, Bull. Soc. franç de dermat. et syph. **34**:726, 1927.

The patient was seen with a chancre of the chin. A Wassermann reaction was negative; results of a dark-field examination were positive. After the fourth injection of neoarsphenamine, there was a sudden bilateral facial paralysis. The observations on the spinal fluid were negative. Treatment was continued with mercury cyanide, in part, because moderate systemic disturbance followed the administrations of neoarsphenamine. A rare disorder was presented under these circumstances. It was attributed to neuritis produced by a Herxheimer reaction.

STREPTOCOCCIC IMPETIGO AND PITYRIASIS ROSEA. L. PERIN, Bull. Soc. franç. de dermat. et syph. **34**:734, 1927.

A case is described in which impetigo bullosa and pityriasis rosea coexisted. The former disease, however, preceded the latter. Bouillon cultures of the scales of pityriasis rosea developed streptococci, a result that the author has obtained in four of seven other cases. He regards pityriasis rosea as of infectious origin; the case presented, as well as other evidence, suggests the possibility that streptococcus is the etiologic agent.

TWO CASES OF NEVOCARCINOMA. LOUSTE, VANOBKSTAEL and CAILLIAU, Bull. Soc. franç. de dermat. et syph. **34**:739, 1927.

In two reported cases, the patient had a melanotic mole on the vulva. In the first, rapid extension in situ and metastasis occurred after excision. Pathologically, the tumor was of mixed Langerhans and "endocrinien" type. The patient in the second case was treated with surgical diathermy with, at least temporarily, a good result. Pathologically, it was almost pure Langerhan's type.

KERATODERMA DISSEMINATUM OF THE HANDS AND FEET IN AN ADULT. P. CHEVALLIER and P. FLANDRIN, Bull. Soc. franç. de dermat. et syph. **34**:743, 1927.

A man, aged 33, who had had the disorder for twenty years, presented acuminate keratotic nodules on the palms, soles and lateral surfaces of the hands and feet. Any other cutaneous anomaly, or systemic disturbance was not demonstrable.

SYPHILIS CONTRACTED WHILE UNDER TREATMENT WITH BISMUTH. M. PINARD, P. VERNIER and MLLE. CORBILLON, Bull. Soc. franç. de dermat. et syph. **34**:745, 1927.

In this instance, the patient had epileptiform attacks. Injections of a bismuth salt were given empirically, as there was not any evidence of syphilis. While undergoing this treatment, the patient developed a chancre. The case

is reported as an example of the inefficacy of bismuth as a syphilitic prophylactic and as a warning against the employment of the drug for that purpose.

THE INTRAVENOUS ADMINISTRATION OF A NEW SOLUBLE BISMUTH SALT: OXYDIETHYLO-DICABOXY-DIIMINO-ISOBUTYRATE OF BISMUTH. JAUSION and PECKER, Bull. Soc. franç. de dermat. et syph. **34**:751, 1927.

This new compound has the advantage of solubility and low toxicity. It contains 41.6 per cent of the metal. The authors have used it for six months on a few patients, with satisfactory results. Experiments on animals indicate that it is valuable.

THE TREATMENT OF PATIENTS WITH PSORIASIS BY THE COMBINED INTRAVENOUS INJECTION OF A NEW ARSENICAL COMPOUND, "EMETIQUE ARSENICAL DE PYRIDINE" AND BISMUTH OXYDIETHYLO-DICARBOXY-DIIMINO-ISOBUTYRATE. DEBUCQUET, JAUSION and PECKER, Bull. Soc. franç de dermat. et syph. **34**:756, 1927.

In the fifteen cases in which the patients were treated by this combination there were no ill effects, and the eruption disappeared in nearly all after from eight to nineteen biweekly injections.

THREE CASES OF ZOSTER OCCURRING IN LEPERS UNDERGOING TREATMENT. LABERNADIE, Bull. Soc. franç. de dermat. et syph. **34**:762, 1927.

Two of the patients were receiving the ethyl esters of chaulmoogra oil; the other, amino-arsenophenol. The authors were unable to find a record of zoster occurring under similar conditions.

MORBILLIFORM ERYTHEMA DEVELOPING DURING TREATMENT WITH ACRIDINE YELLOW. MARCERON and J. IMBERT, Bull. Soc. franç. de dermat. et syph. **34**:766, 1927.

The patient presented a maculopapular eruption, fever and aphthous stomatitis attributed to the use of the drug, which had been given intravenously for chronic gonorrheal urethritis.

CUTANEOUS MANIFESTATIONS OBSERVED DURING TREATMENT WITH ACRIDINE YELLOW. MARCERON, Bull. Soc franç. de dermat. et syph. **34**:769, 1927.

Intravenous injections of this drug are employed in France in the treatment of patients with specific urethritis. The author has noted a number of cases of actinic dermatitis following its use. Morbilliform erythema has also been observed.

PSORIASIS TREATED BY INTENSIVE ULTRAVIOLET RADIATION. BIZARD and MARCERON. Bull. Soc. franç. de dermat. et syph. **34**:770, 1927.

A case of psoriasis is reported in which the patient promptly responded to intensive actinotherapy. A number of remedies, including mild ultraviolet treatments, had failed previously.

ACTIVATION OF PULMONARY TUBERCULOSIS BY ANTICHANCROIDAL VACCINE THERAPY. A. SEZARY and F. BENOIST, Bull. Soc. franç de dermat. et syph. **34**:773, 1927.

In a woman who had arrested pulmonary tuberculosis, activation of that disease followed vaccine therapy (Dmelcos) for chancroid. This method of treatment appears contraindicated in persons in poor health and especially in persons suspected of having pulmonary tuberculosis.

THREE CASES OF LICHEN PLANUS APPEARING DURING NEOARSPHENAMINE TREATMENT. JEANSELME and BURNIER, Bull. Soc. franç. de dermat. et syph. **34**:774, 1927.

A brief report without comment is given of three cases of this type. In one case a new series of injections of arsphenamine caused the disappearance of the eruption; in another case, aggravation ensued.

INTRAVENOUS BROMIDE INJECTIONS IN THE TREATMENT OF ECZEMA AND OTHER PRURITIC DERMATOSES. BURNIER, Bull. Soc. franç. de dermat. et syph. **34**:778, 1927.

Since Lebedjev introduced this treatment in 1924, a number of favorable reports have been published. The author has employed chiefly a strontium bromide preparation. For acute cases of eczema and toxic dermatoses two or three injections have generally sufficed, while in chronic cases, from ten to fifteen injections were often necessary to obtain amelioration. Patients with generalized or localized pruritus (vulvar, anal) have always been benefited. In patients with urticaria, variable results have been obtained. Patients with lichen planus have responded satisfactorily to this treatment. Untoward effects were not observed.

MICHAEL, Houston, Texas.

SWINE ERYSIPELAS AND ERYSIPELOID. L. BAZZOLI, Arch. ital. dermat. e sifil. **2**:449 (June) 1927.

According to the author, swine erysipelas is an infectious disease caused by *Bacillus erysipelatis* of Loefler, which may be transmitted to man through abrasions in the skin, producing an attenuated form of the infection which Rosenbach called erysipeloid.

Man is usually infected when handling meat or animal products, more often during the autumn months, the infection taking place through the lymphatic vessels.

EXPERIMENTAL SUPERINFECTION IN SYPHILIS. A. PASINI, Gior. ital. di dermat. e sifil. **68**:941 (June) 1927.

From the study of seventeen cases of syphilis in which reinoculation was attempted, the author concludes that superinfection is possible in about 70 per cent of cases. The lesions which developed at the site of inoculation were of the same order as those existing, i. e., secondary in patients with early syphilis and deep, ulcerative and destructive in those with late syphilis. Scar tissue from cases of late syphilis failed to produce lesions of syphilis in any patient. The author states that this fact proves that there is a local immunity.

SYSTEMATIZED HYPERHIDROSIS. M. ARTOM, Gior. ital. di dermat. e sifil. **68**:982 (June) 1927.

This article begins with a thorough review of the literature on the pathologic alterations of the secretion of sweat, especially when it occurs in connection with disturbances of the nervous system. The author reports a case of localized hyperhidrosis of the ulnar region of the left hand in a youth, aged 20. The author concludes from the study of his case that hyperhidrosis is due to a disturbance of the function of the sympathetic system.

MELANODERMA TOXICA LICHENOIDES ET BULLOSA (HOFFMANN). E. FREUND. Gior. ital. di dermat. e sifil. **68**:998 (June) 1927.

This is the second case of this rare condition reported by the author. The patient was an Italian worker who had been exposed to fumes of melting tar for several months. The face, neck, abdomen and forearms were the seat of a slate-brown pigmentation of reticular arrangement and lichenoid appearance.

Several spots were present in the conjunctiva. Histologically, hyperkeratosis, perivascular infiltration with numerous chromatophorous cells and free pigment granules were present.

The author believes that the condition is produced by the action of the fumes of tar on the skin. His first case, reported in 1926, had the same etiology.

TINEA DUE TO TRICOPHYTON GLABRUM. G. A. AMBROSSLI, Gior. ital. di dermat. e sifil. **68**:1011 (June) 1927.

Tricophyton violaceum is the most common fungus found in tinea of the scalp in Italy, being present in about 91.72 per cent of cases. According to Sabouraud, *Tricophyton glabrum* is a satellite of *Tricophyton violaceum*. The author reports eighteen cases of tinea of the scalp in which the last mentioned fungus was found.

BLUE NEVUS (BLAUER NAEVUS) OF TIECHE. G. ARMUZZI, Gior. ital. di dermat. e sifil. **68**:1021 (June) 1927.

Six cases of cutaneous lesions of this type are reported. Clinically and histologically, the picture corresponds to the "chromatophoroma" of Tieche. In three cases, chromatophorous cells were found together with nevi cells. In one case, the lesion was of an epithelial nature.

ACUTE NONVENEREAL ULCERS OF THE FEMALE EXTERNAL GENITALS. F. FLARER. Gior. ital. di dermat. e sifil. **68**:1042 (June) 1927.

The author reports four cases of nonvenereal ulcers of the external genitals in girls, one, aged 15 years, and the other three in the first year of life. The nature of these cases was widely different. In one case, tubercle bacilli were found. In the second case, that of the older girl, who had typhoid fever, *Bacillus coli* was found in the pus. In the third case, the lesions were covered with membranous exudate, and diphtheria bacilli were recovered and cultivated. In the fourth case, there was a grave systemic streptococcal infection.

PARDO-CASTELLO, Havana.

ACQUIRED SYPHILIS OF THE INTESTINES. K. NISHIKAWA, Arch. f. Dermat. u. Syph. **153**:539 (Oct. 23) 1927.

Nishikawa describes the pathologic changes noted in six cases from the Rudolf Virchow Hospital in Berlin. In five, the necropsy specimen, in the sixth, the biopsy specimen, was examined; illustrations of the gross and microscopic preparations are given. The jejunum was the chief seat of the disease in two cases, the ileum in four. The colon was involved in two cases. A single focus was present in two cases, in the others, the foci were multiple. All the lesions were annular, even in the one specimen of an early stage. They were flat and sharply demarcated. All showed a tendency to produce stenosis. An observation which he has not met with in the literature was the development of fatty tissue in the serosa in the region of the syphilitic foci. Spirochetes were not found. In two cases, syphilitic lesions were not demonstrable in any other organ. Circumscribed gummatous nodules with central caseation were not seen. The differentiation from inflammatory tumors is not always easy. The main distinction is the absence of the characteristic vascular changes in the inflammatory lesion — endophlebitis and endarteritis productiva obliterans. The veins are involved more extensively than the arteries. Most of the large vessels the author found unaffected, particularly in the muscular and subserous coats. The granulation tissue, proliferating into the lumen of the vessels, takes the greatest part in their obstruction. Proliferation of endothelium and formation of new connective tissue follow and complete the occlusion. It is the proliferation of connective tissue, beginning in the early stage of the disease

and progressing to complete cicatrization, that, together with the disappearance of the characteristic gummatous cellular infiltrate, makes more and more difficult the recognition of the process as syphilitic.

TUBERCULOID LEPROSY. V. KLINGMÜLLER, Arch. f. Dermat. u. Syph. **153**:584 (Oct. 23) 1927.

Klingmüller describes clinically and histologically two cases of tuberculoid leprosy. This is not a clearly demarcated type, as are anesthetic and tuberculous leprosy; it represents, rather, a phase, usually a fairly early one, in the course of the disease. It appears in both the main forms mentioned, but more frequently in the anesthetic form. It is rare that the differential diagnosis from tuberculoid changes of a different etiology — true tuberculosis, tuberculids or syphilis — can be made with certainty. The author's cases show that the histologic peculiarities considered typical of leprosy are not always found Three varieties are known: (1) smooth, flat, erythematous, anesthetic areas, entirely unlike tuberculosis; (2) lupoid spots; (3) abscesses in or near the nerves. The tissue changes show predilection for the connective tissue portion of the skin and nerves; the capillaries near the glands, the muscles and nerves where the subcutis joins the cutis and the capillaries of the papillary portion of the skin are early attacked. In one of his cases, good results were obtained by intravenous injections of platinum. Turpentine injections (intravenous or intramuscular) were to have been tried, but the patient secretly left the clinic. In the other case, surgical excision of the lesions was followed by apparent cure, which continued until the patient's death from heart disease and apoplexy twenty-one years later. Intravenous injections of sodium platinic chloride were found to excite a local reaction in tuberculoid leprosy, as does old tuberculin in tuberculosis.

BEHAVIOR OF ALLERGIC AND NONALLERGIC SKIN EXPOSED TO INFLAMMATORY CHEMICAL OR PHYSICAL INFLUENCES. E. RAJKA and K. POGÁNY, Arch. f. Dermat. u. Syph. **153**:615 (Oct. 23) 1927.

Rajka and Pogány tested fourteen allergic and eighteen nonallergic subjects with roentgen rays, ultraviolet rays, mechanical irritation (dermographism), morphine, epinephrine, oil of mustard, heat and the galvanic current. They found that a parallelism between the reactions to the various stimuli did not exist, i. e., a person who was hypersensitive to the roentgen or ultraviolet rays was not necessarily hypersensitive to heat or chemicals. Attempts to determine beforehand the existence of an abnormal sensitiveness of the skin to irradiation by testing for other allergic reactions would be futile. Fifteen of the subjects were found to have abnormal sensitiveness to the roentgen rays — fourteen were hypersensitive, one hyposensitive. None of these were hypersensitive to ultraviolet rays. Between hypersensitiveness to the roentgen rays and dermographism, on the one hand, and abnormal sensitiveness to morphine, epinephrine and oil of mustard, on the other hand, a certain connection was found to exist, but it by no means amounted to a regular parallelism. Thirty of the thirty-two subjects exhibited an abnormal reaction to one or another of the stimuli employed. The two with normal reactions were in the nonallergic group. The other members of this group were all hypersensitive to at least one of the stimuli, but persons who reacted abnormally to a number of stimuli were fewer in this than in the allergic group.

RELATIONS BETWEEN CLINICAL PICTURES OF SKIN TUBERCULOSIS AND IMMUNITY OF ORGANISM. F. VON POÓR, Arch. f. Dermat. u. Syph. **153**:692 (Oct. 23) 1927.

Poór attempts to establish a parallelism between various manifestations of tuberculosis in the skin and the degree of immunity in the organism. In many cases in which the resistance of the organism as a whole is low, the

skin presents an almost absolute immunity. In another group of persons, the skin is the only organ the immunity of which is lowered. In these persons the characteristic tuberculous lesion — tuberculum anatomicum — appears at the site of infection. In other organisms, the virus spreads and the fight against the antibodies takes place in multiple foci, determined by the variations in structure and in degree of esophylaxis of the skin in different regions. The clinical picture here is that of tuberculids — tuberculosis papulonecrotica when the localization is on the extremities and lichen scrofulosorum when the localization is the follicles. Spontaneous healing is the chief characteristic of this type of tuberculous lesion. It is found in persons with mild, benign general tuberculosis with diminished histogenous skin immunity. The general absence of tubercle bacilli in these lesions and the fact of spontaneous healing are evidences of the capacity of the organism to create immunity. Lupus vulgaris, on the other hand, testifies to a weakened immune biologic reaction capacity. It is found in persons with tuberculosis that is not so mild but is still benign, who have decreased immunity of the skin, and in persons with temporarily decreased immunity of the skin (lupus vulgaris postexanthematicus). In patients presenting tuberculosis miliaris ulcerosa cutis, the organism no longer produces antibodies. The function of immunity is paralyzed. In the skin the bacilli, though present in large numbers, no longer excite a local reaction.

EXPERIMENTAL STUDIES CONCERNING THE RELATIONS BETWEEN THE SKIN AND VITAMINS. W. RICHTER, Arch. f. Dermat. u. Syph. **153**:697 (Oct. 23) 1927.

Six guinea-pigs were fed on a diet from which vitamin C was absent. All died with symptoms of scurvy in from ten to fifteen days. In six other guinea-pigs an area of about 2 sq. cm. on the back was shaved. This was covered with a thick gauze dressing which was attached firmly to the surrounding skin except for a small window cut in its central portion. Into this window, four times a day, the juice of spinach, extracted by pressure by a special method, was dropped until the dressing was saturated. These animals received the same diet as the first six. In from ten to sixteen days, three died with manifestations of scurvy. The remaining three remained well over an observation period of three months. Another series of guinea-pigs were treated in the same manner, except that minerals (potassium, calcium, magnesium, sodium, combined with phosphorus, sulphur and hydrochloric acid, and traces of silicic acid) were added to the spinach juice. The mortality in this group was 30 per cent. In a further series of guinea-pigs, the treatment was the same except that the animals were fed on the vitamin-free diet for from two to six days before the spinach juice was applied to the skin. Regeneration set in within six days in 60 per cent. From the eighth day on, the mortality curve fell rapidly. The comparatively high mortality figures are explained by the complicating infections common in experimental animals. Richter draws the following conclusions: (1) The skin is able to absorb vitamins. (2) From the fact that the spinach juice expressed according to the method used by him contained only slight traces of chlorophyl and that it yet exerted so potent a vitamin action, it must be assumed that the vitamins are not bound to the chlorophyl alone. (3) Since the addition of minerals to the spinach juice considerably improved the results, it appears that minerals have the property of activating vitamins. (4) Regeneration from injury due to lack of vitamins is possible by this method, but only up to a certain degree.

AN IRRITATION PHENOMENON IN ERYTHEMA EXSUDATIVUM MULTIFORME, NOT PREVIOUSLY DESCRIBED. A. PERUTZ, Dermat. Wchnschr. **85**:1481 (Oct. 22) 1927.

In sixteen of the nineteen cases of erythema exsudativum multiforme in which he applied the test, Perutz found that scratching the healthy skin with a needle caused the appearance of an eruption which corresponded in its stage

to the other erythema lesions present in the patient. It never, however, equaled them in intensity. It appeared after about twenty-four hours and lasted for from five to seven days. The fresher the case and the nearer the needle scratch to the exanthem, the more distinct was the reaction.

SOME LESS USUAL SYMPTOMS OF SCLERODERMA. K. VON ARADY, Ztschr. f. klin. Med. **106**:406 (Oct. 14) 1927.

Arady deals with certain lesions caused by scleroderma in organs other than the skin. A knowledge of these rarer localizations is important from the fact that some are early symptoms and may point to the diagnosis before the manifestations in the skin are characteristic. He describes the case of a man, aged 41, in whom scleroderma had led to bilateral opacity of the lens and to characteristic changes in the larynx. There was physical and psychic infantilism, with symptoms typical of hypofunction of the anterior lobe of the pituitary. Absence of anemia and cachexia spoke against pluriglandular insufficiency. A study of the literature shows that sclerodermal cataract does not present a uniform clinical picture; in the case mentioned, it resembled senile cataract. The sclerodermal cataract is always bilateral. It is found chiefly with symmetrical, diffuse scleroderma and appears most often in the third decade of life. It may precede the changes in the skin and be the first evidence of the disease. Rothmund suggested intermarriage among the ancestors of the patient as an etiologic factor. Such intermarriages were present in the case here described. Arady suggests that an altered salt concentration of the body fluids from dysfunction of the vegetative nervous system may affect injuriously the sensitive ciliary cells and the nutrition of the lens, which receives its nourishment from the aqueous humor by osmosis. The larynx and pharynx are somewhat more frequent localizations for scleroderma than is the eye, but only about a dozen cases have been published. The changes are characteristic, but in the beginning are so slight that they are seldom complained of—the voice is slightly hoarse and not so loud as formerly. The changes revealed by laryngoscopy—pallor, slight swelling and vessel dilatation—appear insignificant. In the advanced stage, the atrophy may involve the muscles as well as the mucous membrane. The changes characteristic of scleroderma are shown in insufficient approximation of the vocal cords, caused by shrinking of the adductor muscles. The process is symmetrical, and the clinical picture varies with the muscles involved—the thyro-arytenoidei, crico-arytenoidei and arytenoidei transversi, or a combination of two or of all. In Arady's case, there was a pathologic chink in the region of the pars interligamentosa. In advanced atrophy, the patient speaks in falsetto and with great expenditure of breath, so that after a few syllables the voice becomes aphonic and a new inspiration is necessary. The changes in the larynx occur chiefly in diffuse scleroderma. They are an early symptom. Pharyngeal lesions appear late. They are similar to those of the larynx. Deglutition is difficult. Bulbar symptoms often predominate. In a further case described by the author, scleroderma was associated with a considerable increase in basal metabolism. This was, however, the only one of nine cases examined in which the basal metabolism was abnormal. The specific dynamic action of foodstuffs was found decreased in a number of patients with scleroderma.

CARPENTER, Chicago.

THE USES OF CARBON DIOXIDE SNOW IN COSMETICS. OTTO KREN, Wien. klin. Wchnschr. **42**:1329 (Oct. 20) 1927.

The author takes up briefly the relative values of carbon dioxide snow and radium. He enumerates the various reactions produced by freezing and cautions one to bear in mind factors such as thickness of the skin, involvement of pathologic processes, duration of freezing, and the dangers of overdosage. Carbon dioxide snow is especially valuable in treating patients with small benign superficial anomalies of the skin, as senile keratoses. It is used most

frequently and effectively in treating patients with pigmented and vascular nevi. The various types of nevi, and the results that may be expected in each type are discussed.

RATTNER, Chicago.

GENERAL TREATMENT OF DISEASES OF THE SKIN. M. E. POLANO, Nederl. Maandschr. v. Geneesk. **14**:421, 1927.

In this article, Polano reviews the treatment of diseases of the skin by diet, by internal administration of drugs and by colloid therapy, with particular attention to the mechanism of the curative action. By diet, the sensitiveness of the skin to external stimuli may be altered. Animals with hydrochloric acid poisoning and animals fed on food that has turned sour react with eczematous lesions to irritations which before caused no reaction. Administration of calcium chloride, on the other hand, decreases the sensitiveness of experimental animals to external irritation. The salts contained in vegetables decrease the sensitiveness of the skin to external stimulation, and since common salt appears to oppose the favorable influence of vegetable salts, it should be used as little as possible in the preparation of vegetables. He has seen excellent results from a vegetarian diet in psoriasis. Besides heightening the coagulability of the blood and decreasing the permeability of the vessel walls, calcium diminishes the irritability of the nerves. It is useful in all acute processes, especially in those with exudation. In chronic inflammations, it is not so successful. The relief of pain is a powerful factor in the cure of inflammation. Inflammation of the skin of every kind can be favorably influenced by numbing the sensory nerve-endings in the skin, by either local or central action. The effects of calcium, of cinchophen and of quinine are partly to be ascribed to their analgesic influence. Quinine acts also on the peripheral vessels; in this respect, its action on exudative skin lesions is similar to its action in catarrh of the mucous membranes. Its good effect on pemphigus is probably due to the fact that it slows down protein metabolism; its influence on lupus erythematosus, on the other hand, is probably due to its action on the blood vessels and its checking of cell function, by which it opposes atrophy of the skin. Lebedjew's treatment of eczema with intravenous injections of sodium bromide gave disappointing results in the author's cases. Sulphonated bitumen in combination with vaccinotherapy gave better results than the latter alone in *Staphylococcus albus* infections. The usefulness of arsenic in chronic skin lesions lies in its power to produce hyperemia and thus to further resorption of the inflammatory infiltrates in the deeper layers of the skin; its influence on psoriasis is attributable to its stimulating action on normal cornification. Colloid therapy may be applied in various ways. Venesection is a form of colloid therapy, and its results in exudative diseases of the skin are the same as those of parenteral administration of colloid. When tissue plasma replaces in the vessels the blood withdrawn, the change in the colloidal system of the organism is analogous to that from the introduction of colloid complexes. Not alone the blood-forming organs, but the endocrine glands and the entire metabolism are stimulated. The successful treatment of dermatoses (particularly exudative) with hemotherapy, of erythema multiforme with injections of staphylococcus or gonococcus vaccine is explained by the parenteral administration of colloid plus protein. Many old fashioned popular methods of treatment consisted in the artificial production of inflammation or of suppuration. Their success no doubt depended largely on resorption of the products of protein decomposition from the breaking down of cells. Klingmüller's turpentine injection is a modern form of the same method. Colloid therapy is indicated wherever a good result may be anticipated from decreased permeability of the vessel walls, i. e., in all exudative dermatoses and in hemorrhagic processes in the skin. The action of electrolytes is the opposite. They are used in treatment with the object of "washing" the tissues free of toxins and in the skin diseases of old age (pruritus senilis), probably caused by a scanty supply of blood to the part.

INFLUENCE OF ULTRAVIOLET AND RED RAYS ON THE SKIN. G. J. VAN DEN BOVENKAMP, Nederl. Tijdschr. v. Geneesk. **71**:1617 (Oct. 15) 1927.

Van den Bovenkamp sought to discover the cause of the mutually antagonistic action of ultraviolet and red rays. (It is known that pigmentation and erythema caused by ultraviolet rays disappear under irradiation with red rays—wave length 750-580 millimicrons.) Cantharides plaster, containing cantharides, euphorbin and turpentine, produces similar skin phenomena to those of the ultraviolet ray. Here also there is a period of latency. On each forearm of an experimental subject, a cantharides plaster was applied and left in place for three hours. One arm was then immediately exposed to red rays in a dark room for thirty minutes. On this arm no trace of erythema or blister formation appeared, while on the other arm the usual manifestations occurred and ran a typical course, the redness not disappearing for forty-eight hours. In a further, similar experiment, the plaster was left on for five hours, and the red rays were not applied until four hours after its removal, when intense redness was present and blisters were beginning to form. The rays were applied for forty minutes. In this case, the blister formation took its usual course, but the redness disappeared in twelve hours. Pointing out that the red rays exert their influence in the deeper-lying tissues, the author suggests that, by the hyperemia that they cause there, blood is withdrawn from the superficial tissues, so that the erythema fails to appear or, in case it has already appeared, quickly fades.

CARPENTER, Chicago.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERIAN MEDICAL ASSOCIATION

BEHAVIOR OF GRANULATING WOUNDS OF RABBIT TO VARIOUS TYPES OF INFECTION. C. R. L. HALLEY, A. M. CHESNEY and I. DRESEL, Bull. Johns Hopkins Hosp. **41**:191 (Oct.) 1927.

Experiments made by Halley et al. showed that when, under the conditions specified, a granulating wound in the rabbit was inoculated with a strain of *Streptococcus erysipelatis* which was capable of bringing about an intense inflammatory reaction in a fresh wound, little or no sign of a renewed inflammatory reaction was observed in the surrounding skin area. Furthermore, cultures from such a wound, taken from three to five days after inoculation, indicated that the streptococci disappeared or diminished in number. Somewhat less striking were the results obtained when the granulating wounds were inoculated with *Staphylococcus aureus,* but they tended to show essentially the same phenomenon, although the staphylococci did not disappear so rapidly from the granulating surface as did the streptococci.

ARTERIAL VASCULAR DISEASE OF EXTREMITIES. G. E. BROWN and M. S. HENDERSON, J. Bone & Joint Surg. **9**:613 (Oct.) 1927.

Meddlesome surgery of the toes was the irritating factor in producing gangrene in 50 per cent of the cases reported by Brown and Henderson. They urge that minor surgical measures on the feet of elderly persons, particularly men, must not be undertaken without the condition of the arteries first having been determined. Cognizance of this fact will prevent gangrene in a definite percentage of cases of arteriosclerotic disease.

NATURE OF CANCER: INCIDENCE AND INHERITABILITY. M. SLYE, J. Cancer Research **11**:135 (June) 1927.

Studies made by Maud Slye have yielded several facts of importance: 1. In every respect, the behavior of cancer observed daily for eighteen years was inconsistent with the germ theory of cancer, or with the diet deficiency

theory of cancer. 2. Cancer is not contagious. In the most painstaking and long continued experiments it has never been possible to transmit cancer by contact, whereas all infections here studied have been transmitted by contact. 3. There are apparently two factors necessary for the production of cancer: first, the inherited susceptibility (that is susceptible soil) and, second, irritation or chronic stimulation or trauma of the type fitted to induce it. 4. When irritation to the locally susceptible tissues has been avoided, cancer has not occurred even in susceptible persons. 5. In every phase of this work, including both etiologic studies and studies in heredity, spontaneous cancer has seemed to be due to the lack of a mechanism fitted to control proliferation and differentiation in regenerative growth processes. 6. Cancer then would seem not to be a degenerative process due either to a specific germ or to diet deficiency, though infections or faulty diet might in some cases supply the chronic irritation factor; instead, it would seem to be a growth process, the result of regeneration which is abnormal because of the lack of a physicochemical mechanism fitted to control proliferation and differentiation. 7. The fact of the inheritability of resistance to cancer is one of the few hopeful observations ever made concerning this disease, because it means that, instead of every one being susceptible, large numbers are wholly resistant.

GENERALIZED MYCOSIS DUE TO GLENOSPORA. M. A. BLANKENHORN and J. A. GAMMEL, J. Clin. Investigation **4**:471 (Oct. 20) 1927.

In the case cited by Blankenhorn and Gammel, preliminary symptoms were manifested, and the skin of the chest and face presented local lesions resembling furuncles and so-called deep seated pimples. Finally, the cause of this condition was found to be a fungus of the class *Fungi imperfecti*, subclass *Hyphales*. According to the modus of spore formation, it belongs to order IV, *Conidiosporales* Vuillemin, 1910. Professors Gino Polacci and Arturo Nannizzi considered it a hitherto undescribed species and proposed for it the name of *Glenospora gammeli*. The patient recovered following the administration of potassium iodide and neoarsphenamine.

CONSECUTIVE HERPES ZOSTER AND VARICELLA, WITH VARICELLA IN CONTACT. D. E. H. CLEVELAND, Canad. M. A. J. **17**:1299 (Nov.) 1927.

A case is described by Cleveland in which herpes zoster in an adult is followed after a lapse of time corresponding to the incubation period of varicella by an outbreak of typical varicella in the daughter of the patient, who, as far as could be determined, had not been exposed to other cases of varicella. After a further similar period the patient with zoster, who had never had varicella, developed a generalized rash showing lesions typical of varicella, accompanied by lesions in the lower extremities resembling erythema nodosum. This case is offered as furnishing strong evidence in favor of the theory of a common origin for varicella and a certain proportion of all cases of herpes zoster.

SYSTEMIC FACTORS IN GENESIS OF TAR CANCER. L. KREYBERG, Brit. J. Exper. Path. **8**:352 (Oct.) 1927.

Experimental evidence is presented by Kreyberg which indicates that tar, directly or indirectly, through a systemic factor, influences the skin of white mice, with the result that the incidence of tumor after a certain local insult is increased.

MULTIPLE CAVERNOUS ANGIOMAS OF SWEAT DUCTS ASSOCIATED WITH HEMIPLEGIA. B. W. C. ARCHER, Lancet **2**:595 (Sept. 17) 1927.

The case described by Archer would seem to be one of congenital multiple cavernous angiomas of the sweat ducts, associated with, but not due to, syphilis in a man, aged 30, with a history of two hemiplegic attacks and symptoms of cerebral softening and hypothyroidism.

OUTBREAK OF ERYTHEMA NODOSUM. M. MITMAN, Lancet **2**:751 (Oct. 8) 1927.

The five cases recorded by Mitman occurred almost simultaneously; all occurred in the same London district. In the first two cases there was evidence of direct contact. The outbreak occurred during the prevalence of an epidemic of so-called influenza. In every case except one, the condition was, in the first instance, diagnosed as acute tonsillitis if a gross throat lesion was present, or as influenza if the throat appeared normal.

UNUSUAL LOCALIZATION OF BULLOUS SYPHILIDS IN HEREDOSYPHILITIC INFANT. N. VATAMANU, Ann. d. mal vén. **22**:561 (Aug.) 1927.

In the case of hereditary syphilis reported by Vatamanu, the bullous syphilids were not present until some weeks after birth. They appeared on the scalp, on the face and on the upper part of the thorax. The lesions were not unlike those of impetigo neonatorum, but the microscope revealed spirochetes in the contents of the bullae.

EXPERIMENTAL SYPHILIS IN NEW-BORN RABBITS. S. SHIMODA and M. HONDA, Acta derm.-venereal. **10**:74 (July) 1927.

Experiments made by Shimoda and Honda suggest that the result of syphilitic infection differs according to the method of inoculation. Thirty-three new-born rabbits were inoculated with syphilis either intravenously or subcutaneously in the genitals, with the result that in eleven cases there was clinical manifestation of syphilitic changes. Of ten new-born rabbits receiving virus inoculation intravenously, five developed syphilitic infiltration in the nasal bones on both sides after an average incubation period of forty-two days. Two of these presented, in addition, syphilitic changes in the prepuce and anal regions. Of twenty-two rabbits receiving cutaneous inoculation in the genitals, five developed syphilitic lesions in the genitals (either in labium major or prepuce) after an average incubation of thirty days. One later developed keratitis parenchymatosa without presenting any local lesion. In these six animals, no change developed in the nasal bones or in the anal region.

Society Transactions

MANHATTAN DERMATOLOGICAL SOCIETY

LUDWIG OULMANN, M.D., *Chairman*

Oct. 11, 1927

EPIDERMOLYSIS BULLOSA HERIDITARIA. Presented by DR. BENJAMIN OCHS.

The patient, a baby girl, aged seventeen months, was stated by the mother to have been born with the lesions. When presented, the patient showed bullous lesions on the arms, legs and in the scalp.

DISCUSSION

DR. GOLDENBERG: This case is a typical example of epidermolysis bullosa with atrophic disturbances of the nails. The milium-like epidermal cysts, frequently encountered in this disease, are absent in this patient.

ACRODERMATITIS CHRONICA ATROPHICANS AND SCLERODERMA. Presented by DR. ROSEN.

The patient, a male, aged 32, was born in Russia, married and had no children. He stated that his condition began about five years previous to presentation with a swelling on the wrist. According to the patient's description the swelling coincided with the beginning of a sclerodermatous patch. The process advanced above and below the original area and after a year or so it had involved the entire upper and lower extremities. There were many infiltrations in the skin of the upper and lower extremities and the hands became so stiff that they could not be fully flexed or extended. In addition there was a marked atrophy of the skin over the elbows, knees and regions adjoining the sclerodermatous areas.

The patient had received during the past year a large number of injections of sodium thiosulphate intravenously and, according to his statement, there had been a marked reduction and softening of the inflammatory and sclerodermatous areas. Arsenic in pathologic quantities had been found in his urine and blood before the sodium thiosulphate therapy had been instituted.

DISCUSSION

DR. LEVIN: It is my belief that there is no relationship between the finding of arsenic in the urine and the scleroderma. Nor do I regard the coincidental use of sodium thiosulphate in this case as having been of any benefit in the course of the lesions.

DR. ROSEN: This patient was seen by me in private practice for an extensive gangrenous zoster of the left chest of recent origin. This complication may have been due to the injections of sodium thiosulphate or it may have been a coincidence.

DR. GOLDENBERG: In my opinion, this is a case of acrodermatitis chronica atrophicans.

DR. ELLER: Does Dr. Wise think there are two diseases here — scleroderma and acrodermatitis chronica atrophicans? Several years ago Dr. Wise wrote an article on this subject in which he referred to the differences between scleroderma and acrodermatitis chronica atrophicans. He said scleroderma began with infiltration and terminated with atrophy. Acrodermatitis chronica

atrophicans, he stated, was atrophic in the beginning. This patient presents a definite band of scleroderma on the left wrist.

DR. HOWARD FOX: I think this case can be classed as acrodermatitis chronica atrophicans, in which hide bound lesions are so often seen. I feel rather skeptical, however, about its relationship to arsenic. As to the therapeutic result, I might add that before this could be considered encouraging, the patient will have to show a great deal more improvement.

DR. WISE: In regard to the presence of arsenic in this patient, I cannot conceive of scleroderma having any direct relation to arsenic, due to the fact that in a new-born child, shortly after birth, one sometimes encounters scleroderma; the patient never having had arsenic, nor the mother.

In acrodermatitis atrophicans we find that the infiltration of the skin occurs not primarily, as it does in true scleroderma, but that it is a secondary manifestation and follows the atrophy. The so-called scleroderma in this disease takes place at the site of skin which has already passed through the stage of atrophy. It is called pseudo-scleroderma by the German and Austrian writers. In Kyrle's book on histopathology, several points are brought up with regard to differences in the texture, arrangement and distribution of the elastica in this pseudo-scleroderma, as compared with the elastica in true scleroderma.

LUPUS VULGARIS. Presented by DR. GILMOUR.

The patient, L. C., white, female, widow, aged 77, stated that shortly after having had scarlet fever at the age of eight years, lesions developed on her body which remained present until the time of presentation. The patient showed thin, rather white scar tissue over the entire back of the lower half of the right forearm and extending over the radial side to the middle of the flexor surface of the forearm. The lower limit was the middle of the hand on the dorsal surface and the base of the thumb, on the flexor surface. The lower border showed active lesions with apple-jelly nodules present. Blood and spinal fluid Wassermann tests were negative.

DERMATITIS VEGETANS AND TERTIARY SYPHILIS. Presented by DR. ELLER.

The patient, a male aged 62, from the Post-Graduate Skin Clinic, stated that the skin of both legs had been entirely clear until about five years previous to presentation, at which time he had injured the right shin. This had caused an open sore which soon closed. Following this the leg remained in good condition but had itched considerably. Subsequent to long-continued scratching a large crusted, moderately superficial ulceration appeared which persisted for the five or six months prior to presentation. About the same time the heel had also become involved, having commenced with a superficial ulceration covered by dark yellow crusts and which had steadily progressed until the whole heel became affected. When presented, there was a large cauliflower-like excrescence on the outer side of the heel. The patient gave no history of syphilis. A microscopic study of a section showed changes characteristic of dermatitis vegetans. The Wassermann reaction was strongly positive.

DISCUSSION

DR. WISE: I think the diagnosis of dermatitis vegetans is quite applicable to the lesion shown here, but the patient has varicose veins and a four plus Wassermann reaction, and it is possibly a syphilitic keratosis due to the poor circulation induced by the varicose veins.

DR. MACKEE: Some of the clinical features are suggestive of syphilis and the entire process may be syphilis or a secondary condition on a syphilitic base. On the other hand there are some clinical features here that do not resemble syphilis, such as the wide-spread exudation, the vegetating dermatitis, etc. It is possible that we have syphilis developing on varicose eczema or dermatitis hemostatica.

Multiple biopsies and a therapeutic test should establish the diagnosis. The positive Wassermann reaction does not signify anything more than that the patient has syphilis.

DR. HOWARD FOX: One striking feature in this eruption is its unilateral distribution. A granulomatous process, consisting of grouped nodules with sharp demarcation in places, upon one foot suggests syphilis or tuberculosis. The fact that the Wassermann test is positive makes it quite probable that the process is syphilitic. In my opinion it will disappear entirely under anti-syphilitic treatment. In regard to the relationship of varicosities to this eruption it should be recalled that most cases of varicose dermatitis, if unilateral, are more apt to occur on the left leg. The eruption in this case affected the right leg.

DR. LEVIN: This is the type of lesion we used to see at the Beth Israel and City Hospitals. I think this is a chronic eczema with secondary changes, and hypertrophy of the tissues. The leg is enormously enlarged from the chronic edema resulting from the poor vascular condition. I do not see any clinical evidence of syphilis. I doubt whether antisyphilitic treatment would affect the condition.

DR. SATENSTEIN: I think this is the type of process that is always secondary to some other condition. The worst case of the kind I have ever seen was in a case of dermatitis herpetiformis. What the underlying condition is or was in this case I do not know. The patient now presents a secondary dermatitis with papillomatous and verrucous formation.

DR. GOLDENBERG: In reference to the remarks made by Dr. Satenstein, that the vegetating masses are due to a secondary infection, I would like to draw your attention to the fact that a constitutional factor may explain their presence. It has been pointed out by Herxheimer, a number of years ago, that they may develop on any skin lesion, eczema, lichen planus, psoriasis, etc. The individual bears in himself this tendency.

RAYNAUD'S DISEASE OR SCLERODERMA. Presented by DR. GEORGE ANDREWS.

The patient, a female, aged 40, born in Poland, had come to the United States at the age of twenty. According to her statement the lesions had developed while she had been living in Poland, having commenced with a sense of numbness in the hands accompanied by spells in which the hands had become white and practically exsanguinated, then becoming blue. There had been no pain at any time but the hands had felt numb or dead. The condition had gradually developed accompanied by atrophy of the hands and fingers and ulcerations on the ankles which had healed and then broken open over a period of seven years. One lesion had remained an open sore on the ankle for two and a half years prior to presentation.

Microscopic examination of tissue excised from the edges of the ulcer showed some round cell infiltration but no evidence of granuloma. The patient had had about seven Wassermann tests made, all of which had been negative. She had also been given a course of antisyphilitic treatment. There were no objective sensory disturbances. The patient had some changes on the nose where the skin looked atrophic at the time of presentation, and the ulcerations on the tips of the fingers were symmetrical.

DISCUSSION

DR. LEVIN: This is a case of sclerodactylia, occurring in a case of generalized scleroderma. I see no clinical evidence of Raynaud's disease.

DR. GILMOUR: I think that it is scleroderma.

DR. GOLDENBERG: This is scleroderma (sclerodactylia) with the so-called Raynaud syndrome, which we encounter quite frequently.

DR. HOWARD FOX: I agree entirely with Dr. Goldenberg's conception of

this case. It appears to be an ordinary scleroderma of the sclerodactylia type with associated Raynaud's phenomena. It is by no means uncommon for the latter condition to be seen in this form of scleroderma.

DR. MACKEE: It is not common to have manifestations of scleroderma in Raynaud's disease. I think that this is scleroderma.

DR. FRED WISE: My conception of this case differs from most of the others. I think it is a typical case of Raynaud's disease with acroasphyxia and sclerodactylia. Most cases of Raynaud's disease, advancing as this has, show a puckering of the chin not seen in ordinary scleroderma. Trophic ulcers do not mitigate against the diagnosis of Raynaud's disease.

I make the diagnosis on the history of acroasphyxia and sclerodactylia and the puckered chin characteristic of Raynaud's disease. There is often difficulty in differential diagnosis between Raynaud's disease and scleroderma.

DR. LEVIN: This patient presents a characteristic picture of sclerodactylia with infiltration of the skin and decreased mobility. The face shows the typical mask-like expression. The nose is beaked. The skin is very taut. The extremities show firm, hard, drawn skin, which is most marked on the fingers where the skin is so tense as to make the movement of the parts difficult. Raynaud's disease is a classical syndrome. It shows the three stages of asphyxia, syncope and final ulceration. It depends on a vasomotor disturbance in which the blood vessels are constricted as a result of spasm and relaxation. As a result there is a loss of tone, giving rise to the drawn, bluish, tense features, with immobility and with cyanosis. The ulcers are the result of trophic disturbance. In scleroderma we have an entirely different picture. Here we have a decreased blood supply and secondary ulceration due to the fact that there is an intense infiltration with connective tissue formation around the blood vessels, compressing the blood vessels and interfering with circulation. We should always bear in mind, it seems to me, that although these conditions strongly resemble each other, they are entirely different in nature. The development and causation make them different.

DR. WISE: It seems to me a differential diagnosis between the two diseases should be established and I should like this patient to be examined by a neurologist.

DR. MACKEE: I wonder if it is correct to interpret the ulcer on the ankle in this patient as trophic. It does not seem to me to be what I have been taught is a trophic ulcer. It seems to be a vegetating lesion with ulceration.

DR. WISE: I thought it was a trophic ulcer for the reason the circulation has been impeded by acroasphyxia but whether atrophic ulcer such as is obtained in leprosy or syphilis, I could not say.

DR. HOWARD FOX: I cannot agree with Dr. Wise that scleroderma necessarily follows Raynaud's disease. The two conditions may be associated or occur independently. I have followed a classic case of Raynaud's disease for many years and have presented the patient before this Society. She has never shown any suggestion whatever of scleroderma.

DR. OULMANN: Would not roentgenograms help to establish the diagnosis?

DR. MACKEE: A roentgenogram would show atrophy of bone but there would be nothing sufficiently characteristic to be of value in differential diagnosis. I doubt if a diagnosis could be established in this way.

DR. ANDREWS: The biopsy showed only a marked acanthosis and beneath in the papillary zone moderate round cell infiltration, such inflammation as one finds beneath an ordinary callous. There were no changes suggestive of granuloma. The nervous symptoms of Raynaud's disease, i. e., tingling, numbness and spasms, are accompanied by protracted periods of remissions in which the patient is free from any sickness.

LUPUS VULGARIS. Presented by DR. ROSEN.

The patient, T. R., a woman, aged 30, born in Germany, married, said that a small lesion developed on the left side of her chin about nine years previous to presentation which persisted and resisted all forms of treatment. At the time of her admission at the Post-Graduate Hospital Clinic the involved area had become so irritated by local applications that it was difficult to make an absolute diagnosis. It was possible, however, to recognize two or three small nodules in the affected area. One of these was removed and the microscopic examination revealed the typical picture of lupus vulgaris. The interesting feature was that two or three weeks after the healing of the biopsy wound, the entire lesion had involuted. The patient, however, had also received five injections of gold thiosulphate and the question arose whether the biopsy or the treatment had influenced the lesion.

DISCUSSION

DR. SATENSTEIN: Lupus vulgaris is not supposed to respond to gold therapy; lupus erythematosus responds very well. I was surprised at the rapid results in this case.

DR. WISE: I have little doubt that the cure of the case is due to the gold injections. Evidently some cases of lupus vulgaris respond to that type of treatment and others do not. This one probably did.

DR. MACKEE: There is voluminous literature on the subject of the gold treatment of lupus erythematosus. During the past year there has been an increasing number of reports on the gold treatment of other dermatoses of the tuberculosis group. There is enough evidence now in the literature to warrant the use of gold cautiously in lupus vulgaris. Many cases have been cured or improved. I think one can at least believe it possible in this case that gold was responsible for the disappearance of the nodules. The cases so far reported of lupus vulgaris that have responded to gold are of the type with fairly active nodules, not the atrophic or sclerotic type, with small deep-seated nodules.

DR. BECHET: I am very much interested in Dr. MacKee's remarks because my experience with the gold treatment coincides with his statements. I had a disseminate nodular type of lupus vulgaris that became well under gold treatment, but in two other cases of lupus vulgaris it had no affect at all.

D. L. SATENSTEIN, M.D., Secy.

DETROIT DERMATOLOGICAL SOCIETY

Regular Meeting, Oct. 18, 1927

H. S. BARTHOLOMEW, M.D., *Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. SCHILLER and DR. SCHLEGELMILCH.

B. B., a boy, aged 11, presented a nonpruritic eruption of seven months' duration on the forearms, back, thighs and legs. There were a large number of somewhat depigmented medium to large coin-sized circular and oval patches, sharply outlined and composed of tiny, scale-capped, follicular papules. Some of the patches had become erythematous during the period of observation, and all were devoid of hair.

DISCUSSION

DR. SCHLEGELMILCH: There are signs of dermatophytosis about the toes.

DR. WILE: This peculiar eruption is probably not of vegetable parasitic origin. It is composed of pinkish, follicular, hyperkeratotis lesions, and it may

be an unusual case of lichen scrofulosorum or possibly pityriasis rubra pilaris. A diagnosis of dermatophytosis would be easy to prove.

DR. PARKHURST: I favor a diagnosis of pityriasis rubra pilaris, although the configuration of the patches and the involvement of the hair is suggestive of trichophytosis. Cultural and microscopic examinations should be made.

DR. JAMIESON: The history of the case is against a diagnosis of tinea and in favor of pityriasis rubra pilaris.

DIFFUSE SYMMETRICAL SCLERODERMA. Presented by DR. SCHILLER and DR. SCHLEGELMILCH.

F. H., a housewife, aged 55, had first noticed hyperpigmented patches on the face, neck, arms and legs two years previously, hyperesthesia about the neck one year previously, and stiffness of the neck eight months before presentation. Infiltration of the skin was noted especially about the forehead, neck, upper part of the chest, shoulders and arms, and the border of the affected area was erythematous. Many portions of the sclerodermatous area were atrophic. There were small pea-sized erythematous macules on the palms and hyperpigmented areas on the soles. The patient had lost 60 pounds (27.2 Kg.) in the previous two years, but a physical examination did not reveal any abnormality. The blood count was normal and the Wassermann reaction was negative.

CIRCUMSCRIBED SCLERODERMA. Presented by DR. SCHILLER and DR. SCHLEGELMILCH.

R. S., a housewife, aged 44, had had both ovaries removed four years previously, on account of tumors. About nine years before presentation, she had first noticed thickening and pigmentation of the skin of the nucha. Extending as a band, the thickened area gradually encircled the neck during the next five years, spreading toward the ears and over the clavicles. The skin was firm and apparently edematous, and at times there was a sensation of burning.

DISCUSSION

DR. WILE: The first case especially shows the preliminary edema, sometimes erythematous, similar to that seen in early acrodermatitis chronica atrophicans.

ONYCHOMYCOSIS (?). Presented by DR. SCHILLER and DR. SCHLEGELMILCH.

Mrs. W. A., aged 36, a washerwoman, had first noticed brittleness and pigmentation of the right thumbnail four years previously. The nails of the right middle finger, left thumb and left forefinger were subsequently involved, with considerable thickening and numerous transverse ridges. There was some pain and itching about the nail-beds. The examination of scrapings had been negative for vegetable parasites.

BLASTOMYCOSIS. Presented by DR. SHAFFER.

E. G., a negro, aged 48, a waiter, had noticed a small nodule on his nose four months previously; it had gradually enlarged. On the end of the nose there was a cauliflower-like vegetating mass, involving the entire bulbous portion and extending to the middle of the bridge. On pressure small pus droplets exuded from small openings. *Blastomyces* were found in a potassium hydroxid preparation, and the biopsy observations were those of blastomycosis. The Wassermann reaction was negative.

A Case for Diagnosis. Presented by Dr. Troxell.

F. W., a teamster, aged 62, had first noticed a small swelling of the right side of the lower lip following a bruise, five months previously. Growing rapidly, the mass had broken down, and when first seen four weeks before presentation, the entire right half of the lip had been involved. The mass was of granulomatous appearance. Subjective symptoms had been slight, the patient's general health had been good, and there had been no loss of weight. He had smoked a pipe for years, holding it in the right side of his mouth. He had had a penile sore at the age of 18, followed by mixed treatment. The Wassermann reaction was strongly positive. Considerable improvement in the lesion on the lip had followed two injections of neoarsphenamine. The diagnoses of cancer or gumma were being considered.

DISCUSSION

Dr. Troxell: The original diagnosis was cancer, but the Wassermann reaction, being positive, suggested antisyphilitic treatment before the operation.

Dr. Parkhurst: This mass lacks the infiltration of a syphilitic lesion, and seems to be a prickle cell epithelioma. The administration of arsenical drugs might hasten the proliferation of such an epithelioma, and should therefore be avoided.

Neurotic Excoriations. Presented by Dr. Wollenberg.

M. W., a housewife, aged 65, had always been subject to attacks of pruritus, the last attack having begun in July, 1927, and continued until the time of presentation. The trunk, arms, legs and feet showed many scars from old deep excoriations, and especially on the legs and feet there were many freshly crusted excoriations with inflammatory areolae, and small patches of hyperpigmentation.

Tinea Versicolor. Presented by Dr. Van Rhee.

M. L., a housewife, aged 42, had first noticed an eruption on the chest four weeks previously. A large number of fawn-colored macules, single and confluent, were found over the sternum and abdomen, under the breasts, in the axillae and in the pubic region. There was faint scalling and many small erythematous papules were present. *Microsporon furfur* was found in the scrapings. The unusual feature of the case was its active inflammatory aspect.

Grouped Follicular Secondary Syphilid. Presented by Dr. Schiller and Dr. Schlegelmilch.

L. W., a housewife, aged 31, gave a history of infection in April, 1927, with a vaginal chancre and generalized eruption appearing in May, and persisting. The distribution of the eruption was still fairly general. There were many coin-sized groups of tiny scale-capped follicular papules. There was nocturnal pruritus. The syphilitic eruption involved the mouth and palms also, and the lymph nodes were enlarged. The Wassermann reaction was strongly positive.

DISCUSSION

Dr. Wile: This is the sort of case commonly mistaken for something else. There is a striking resemblance to seborrheic dermatitis.

Ichthyosis, Dermatophytosis and Erythema Multiforme. Presented by Dr. Schiller and Dr. Schlegelmilch.

K. L., aged 12, and her brother, A. L., aged 3, presented a generalized dryness and scaling of the skin, especially on the arms, buttocks and legs, present since birth. The skin of the parents and other relatives was said to

be normal. The girl also had dermatophytosis of the feet and wrists, of several months' duration, and fading violaceous patches on the forearms which had improved with the administration of sodium salicylate.

A Case for Diagnosis. Presented by Dr. Troxell.

C. L., a mechanic, aged 40, presented a generalized lipomatosis which had begun at the age of 20 and slowly increased. Ten days previously a lesion had appeared on the right side of the dorsum of the tongue. It was a dime-sized, infiltrated, rough, fissured area, without subjective symptoms. Huskiness of the voice had first been observed two months previously; a laryngeal examination had not been made. A positive diagnosis of active pulmonary tuberculosis had been made about one year previously. The Wassermann reaction was negative.

DISCUSSION

Dr. Shaffer: The lingual lesion is hard on palpation, and is painless, both features being against a diagnosis of tuberculosis. A diagnosis of malignancy or chancre should be considered.

Dr. Wile: The mass feels like a gumma of the muscularis. It does not look like a cancer or chancre. A tuberculous lesion is fissured, red and tortuous, with white points, and is painful. I should call this a gumma.

Dr. Jamieson: I agree with a diagnosis of gumma.

Symptomatic Purpura. Presented by Dr. Valade.

F. A., a baker, aged 36, born in Germany, had had an operation for an abscess of the lung in August, 1927. In February, 1927, a "shower" of red spots appeared on his skin, without malaise or fever; this eruption disappeared in April. In September, four weeks after the operation, there was a second cutaneous outbreak. On both legs and the right thigh there were many red, yellow and brown puncta, tending to form a reticular network. There were also some slightly infiltrated red macules varying in size from that of a pinhead to that of a pea. Atrophy or telangiectasia was not found, nor was the involvement especially follicular. Cardiac examination revealed a systolic murmur and a blood pressure of 186 systolic and 132 diastolic. The Wassermann reaction and urinalysis were negative.

A Case for Diagnosis. Presented by Dr. Jamieson.

W. D., a man, aged 32, a restaurant proprietor, for one and one-half years had had an enlarging group of slightly elevated, nonpruritic, faintly erythematous plaques over each malar bone. New lesions had appeared over the forehead. The general health was good, there being no infections except a slight pyorrhea about the lower central incisor teeth.

DISCUSSION

Dr. Shaffer, Dr. Parkhurst and Dr. Keim agree on a diagnosis of lupus erythematosus.

Tuberculosis or Madura Foot (?). Presented by Dr. Jamieson.

S. M., an Italian laborer, aged 35, in good general health, at the age of 5 years had first noticed a swelling of the right foot and ankle, with sinus formation ensuing. This persisted for some time, and the sinuses drained; then the symptoms subsided, but the foot did not return to its normal size. About one year prior to the time of presentation, following an injury, the same symptoms had recurred, and the patient was first seen in May, 1927. At that time the appearance was typical of Madura foot, but granules could not be found in the pus, macroscopically or microscopically. There was enormous

enlargement of the foot, ankle and leg, with a number of open sinuses, and an abscess in the calf of the leg. A biopsy report stated that the tissue was tuberculous, and roentgenologic examination showed marked destruction of the tarsal and metatarsal bones. Smears, cultures and inoculations were negative for all organisms. The Wassermann reaction was negative. Three months of ultraviolet therapy, with potassium iodide in increasing doses had been followed by a considerable reduction in the swelling, an almost complete cessation of suppuration, and freedom from pain.

DISCUSSION

DR. KEIM: I saw a similar case last winter. It was at first called a Madura foot, but after amputation it was found to be tuberculous.

CHRONIC RADIODERMATITIS WITH CARCINOMATOUS DEGENERATION. Presented by DR. HASLEY.

C. T., a housewife, aged 36, born in Finland, had had a lesion on the right cheek since birth. It was subjected to about twenty roentgen-ray treatments during 1912 and 1913, and remained well for nine years, when an ulcer appeared after the extraction of a tooth. The ulcer had persisted, and two weeks before presentation a small nodule had developed, growing rapidly.

H. J. PARKHURST, M.D., Reporter.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, Oct. 19, 1927

FRANCIS EUGENE SENEAR, M.D., *Presiding*

PEMPHIGUS VEGETANS. Presented by DR. BEESON.

A Swedish man, aged 60 stated that his disorder began in January, 1927, with a "sore mouth." Shortly afterward lesions appeared on the trunk, about the genitalia and in the axillae.

The lesions on the body had cleared up considerably following roentgenotherapy, but were now recurring.

DISCUSSION

DR. ZEISLER: I believe that the diagnosis is correct, and it is my impression that pemphigus is increasing in the Jewish race. I have had four cases in adult Jews during the past summer.

DR. LIEBERTHAL: It is true that the majority of cases of pemphigus occur in the Jewish race. The only case I have seen in a native born American occurred several years ago.

DR. O'LEARY: Some of the members present probably remember the enthusiasm with which several of the Pittsburgh dermatologists recommended the use of direct transfusions of whole blood in the treatment of pemphigus. Since May, 1927, we have treated two patients with chronic pemphigus by this method without any apparent therapeutic benefit.

DR. OLIVER: This patient was on our service at the Cook County Hospital for one and a half months. He looked much better at the time of presentation than he did at the hospital.

DR. LIEBERTHAL: Referring to Dr. O'Leary's remarks, I read a paper by Linsir of Tuebingen, who has been using normal human blood serum in cases of pemphigus with good results. His procedure is far simpler than the ordinary

blood transfusion and I think could be readily carried out, particularly in the patients who are helpless. It seems to me it would be worth while to try it.

DR. STILLIANS: I have been trying out plasmochin, a new drug for the treatment of malaria. I was told by letter of brilliant results from this treatment in Vienna. I tried it with quinine and then without quinine, and thought I got temporary improvement. I have not had bad results but the improvement is only temporary, and I have learned recently that the results abroad have not been as good as they were thought to be at first.

CASE FOR DIAGNOSIS. Presented by DR. STILLIANS.

A girl, aged 10, presented a disorder of eight years' duration, which started as an eruption on the hands and forearms. A year later it spread to the face and lower extremities. The lesions varied in extent, sometimes almost disappearing. Itching was intense. There was a yellowish pink, densely set, symmetrical, papular eruption, on both cheeks which was not sharply defined; on the forearms, there were a few groups of tiny papules with numerous scratch marks. Vesicles were not present, but on previous occasions pea-sized, discrete vesicles had been observed on the flexor surface of the left forearm just above the wrist. These sprang from the apparently normal skin and did not rupture easily; they disappeared spontaneously in a few days.

DISCUSSION

DR. O'LEARY: The picture presented by this child is that of a chronic eczematoid dermatitis. The distribution suggests the possibility of an allergic factor as the cause of the dermatitis. The picture is so distinctly one of eczematoid dermatitis that I do not believe the diagnosis of hydroa estivale is justified.

DR. MCEWEN: I think it is a case of protein sensitization, both from the history and the type of lesions. In my opinion, the care of the patient should include a complete skin test with the proteins and epidermals, and then the exclusion from the diet and from contact of the things to which the patient is sensitive.

DR. PARKHURST: The location of the lesions on the face, with the total absence of them on the forehead and over the ears, which were covered by the hair, was somewhat suggestive of photosensitization.

DR. ZWICK: It was suggested that the diagnosis of dermatitis herpetiformis might have to be considered

At the time of my connection with Jadassohn's clinic in Berne, a diagnostic test was worked out with iodide of potash ointment. The iodide (applied in suitable concentration) produces a characteristic eruption of vesicles on the skin of patients with Duhring's disease. The procedure is, at times, of value in the differential diagnosis of Duhring's and other vesicular skin diseases.

DR. STILLIANS: We were interested in this case because of the persistent lesions on the cheeks, which did not yield to soothing or stimulating remedies, as ordinary dermatitis should, and because the child sometimes has discrete vesicles on the arms and legs which remain only a short time. She did not have any lesions when she was presented. The mother said that they occurred in periods of about five weeks apart, and are few in number. We will try to work up the case.

CASE FOR DIAGNOSIS. Presented by DR. SENEAR and DR. WIEN.

L. E., a negress, aged 47, stated that she had had a group of enlarged cervical glands at 7 years of age that had broken down and discharged for one year. At 14 years of age she had noted "lumps" all over her body that appeared about four to six weeks after her marriage and persisted for months, finally involuting spontaneously, leaving numerous superficial, coin-sized scars. At intervals for

the past nine or ten years new lesions had occurred on the trunk and extremities. When the patient was presented there were indolent purplish nodules on both lower extremities that had been present for one month and which were moderately painful. There were also indolent pea-sized lesions on the backs of both hands and forearms, in various stages of involution. Small, glistening papules were present on the back of the neck and region of the upper part of the shoulder that had been present for four years.

The patient had a moderate cough that had been present for some time and she expectorated a moderate amount of sputum, which was not blood tinged. The history did not reveal any recent loss of weight, night sweats or rise of temperature in the afternoon. The family history was negative for tuberculosis. The blood Wassermann reaction was negative. She gave a history of three spontaneous miscarriages, at six, seven and nine months, respectively. Physical examination of the chest was negative for signs of recent or active tuberculosis.

DISCUSSION

DR. MICHELSON: I think that the woman has a systemic tuberculosis with a variety of tuberculous lesions of the skin.

DR. FINNERUD: My impression was the same as that of Dr. Michelson's.

DR. ZWICK: The impression which I received from the rather brief examination of the condition led me to suggest a tentative diagnosis of anetodermia. I found both striate or elongated and rounded maculae on the extensor surfaces of the legs and arms of this colored patient and also on the nape of the neck. The maculae were slightly depressed below the surface of the surrounding skin. Their surface was peculiarly soft and smooth, and, by slight manipulation, could be thrown into minute wrinkles or folds. The palpating finger did not meet any resistance and sank, as it were, into the depressions. To support my diagnostic suggestion of the condition, histologic examination ought to show an absence or diminution of elastic fibers. I have never had the opportunity to examine an anetodermia in a colored person.

DR. FOERSTER: I would make a diagnosis of tuberculosis cutis, represented by various types of benign tuberculous lesions as one would expect to find them under conditions in which bacilli disseminated from an internal primary focus encounter a highly developed cutaneous protective mechanism. There was a notation in the history that evidence of tuberculosis was not found on physical examination. I think some evidence may be found in the chest on roentgen-ray examination, which frequently reveals lesions at the hilum and in other areas not demonstrable by other means.

DR. SENEAR: I would like to have someone express an opinion of the lesions on the shoulders, which are apparently a part of the process. We saw the patient for the first time the day before presentation, and our opinion was in accord with that expressed at this meeting. However, we were interested in the possibility of lichen nitidus in the lesions on the neck with the several types of tuberculous lesions presented elsewhere. We had never seen it in the colored race, but wish to consider the possibility. We will try to report later from the histologic standpoint.

EPITHELIOMA, PAGET'S TYPE (?). Presented by DR. OLIVER and DR. FINNERUD.

A man, aged 63, was previously presented before the Society with the diagnosis of Bowen's precancerous dermatosis. The condition had been present for fifteen years, beginning as a small scab or scale, which would peel off and then form again. When first seen, in April, 1927, he presented a large lesion the shape and size of a saucer on the left side of the abdomen, the surface of which was red, oozing and granular in appearance. While in the hospital his prostate was removed but nothing was done for the lesion of the skin. He had now returned after five months' absence.

On the right side of the abdomen there was an area of superficial ulceration the size of a large saucer. The base was granular and there were two large plum-sized tumors present on this area.

DISCUSSION

DR. MICHELSON: I think that the terms, Bowen's precancerous dermatitis and Paget's disease, are both confusing. The conditions are both potentially cancerous, rather than precancerous. I think the present condition is already malignant.

DR. HARRY R. FOERSTER: I consider the lesion clinically and histologically a Paget's type of epithelioma.

DR. STILLIANS: Clinically the condition was an epithelioma. I did not see the section.

DR. FINNERUD: The case clinically and histologically is identical with a case Dr. Ormsby showed at the annual meeting in 1924, except that his patient had two such patches instead of one and the duration was about thirty years, while in this case the duration has been fourteen years. Each condition began as a scaling red patch, in the center of which tumors developed. The first patient is now dead, apparently as the result of metastases in the mediastinum and axillae. We have sections of true carcinoma from that case, and the histologic picture from the center of the patches was exactly the same as in this case. There is a marked dyskeratosis and cornification in the individual cells. There is mitotic division both in the margin of the cells and in the tumor itself. I think it is a form of squamous cell epithelioma which apparently will terminate fatally.

PITYRIASIS RUBRA OF HEBRA (?). Presented by DR. OLIVER and DR. FINNERUD.

A man, aged 46, was admitted to the Cook County Hospital on Sept. 14, 1927, complaining of itching and redness of the skin of one year's duration, which had begun with red spots on his arms. He thought at that time that the trouble was due to some lye which he used in cleaning the grease from machinery. The eruption rapidly extended to the upper part of his arms, then to his buttocks and face, and finally involved the entire body. Itching was intense, and he stated that he had experienced chilly sensations for four or five months before consultation. The history did not reveal any intravenous medication.

The entire body was involved in an exfoliating dermatitis. The skin was inflamed and scaly and on the palms and folds of the skin there was considerable thickening. On September 19, the blood count showed 8,000 white blood cells, 83 per cent polymorphonuclears, and 17 per cent lymphocytes.

DISCUSSION

DR. WILE: It is difficult to accept a diagnosis of pityriasis rubra unless one had seen this case from its beginning and followed it to its end. At this moment it is merely a case of exfoliative dermatitis. The thickening of the skin, and the associated glandular swelling, make up precisely the picture that one can get in exfoliative dermatitis from many different conditions, such as arsphenamine dermatitis, leukemia, lymphosarcoma and similar disturbances.

DR. HARRY R. FOERSTER: I agree with Dr. Wile and see nothing to substantiate the diagnosis which was offered.

DR. PUSEY: I have been wondering for some time if pityriasis rubra of Hebra should not be abandoned as a definite conception. It is simply an exfoliative dermatitis with enlarged glands, and the only thing that separates it from other cases is that it persists. I imagine that Hebra in describing this condition included a number of cases of universal exfoliative dermatitis of

many origins such as Dr. Wile mentioned, and I have doubted several times as to whether the name is entitled to be preserved, except as a descriptive term.

DR. WILE: I have seen several of these cases which have ended fatally. At the postmortem examination a varied number of conditions have been found. In some cases, true lymphosarcoma infiltrates throughout the body, in others, leukemic and in still others, unclassified forms of lymphoblastomas. I believe that the fatal cases described by Hebra under the name of pityriasis rubra were probably cases of lymphoblastomata, with the extraordinary exfoliative dermatitis which accompanies these conditions. I am entirely in accord with Dr. Pusey's idea that the term — pityriasis rubra of Hebra — might well be abandoned.

DR. OLIVER: Dr. Finnerud and I presented the case with this diagnosis to stimulate discussion. The man has been under observation for three or four weeks. He is a machinist and said that the disorder began about a year prior to presentation as red spots on his arms, face and neck after the use of lye for cleaning his machinery. It rapidly spread to the rest of the body. He did not give any history of taking arsenic or other drugs. The case can be called an idiopathic exfoliative dermatitis. The patient is on Dr. Zeisler's service and we have all considered it an unusual exfoliative dermatitis.

DR. MICHELSON: One frequently sees cases of generalized exfoliative dermatitis and it is most difficult to arrive at the etiology. The diagnostic procedures that one follows usually include blood study, biopsy of the skin and excision of a superficial gland, especially the inguinal. I should like to emphasize that none of these procedures give information at times, that it is pathognomic, and that one positive blood smear for leukemia, or a report of Hodgkin's disease from the glands should not be accepted as final. The biopsy of the skin, when positive for a known condition, is more valuable than the pathologic diagnosis of the gland.

DR. LIEBERTHAL: I have always found that one can differentiate this type of dermatitis of Hebra from the other exfoliative forms. In the first place there is never any thickening of the skin; it is always thin. The desquamation consists of fine scales; the atrophic development begins at an early stage and there is a third point which should not be overlooked, and that is the pigmentation. As intense progressive pigmentation is not observed in any form of dermatitis exfoliativa as in the type known as Hebra's. The fact must not be overlooked that they all belong in the same group.

DR. BECKER (by invitation): I agree that there is a distinction between pityriasis rubra (Hebra) and exfoliative dermatitis; neither condition is a disease entity, but rather a sign of one of many internal disorders. I believe the case under discussion is one of exfoliative dermatitis.

DR. FINNERUD: I have seen this patient two or three times in the past month and told Dr. Oliver that I was not impressed at all with the diagnosis of pityriasis rubra of Hebra, and neither was he. The only resemblance to this disease that I could see was that the patient has a mahogany brown color in a poor light.

DR. ZEISLER: This patient has not been observed long enough for one to make a definite diagnosis. It is perfectly evident that he has an exfoliative dermatitis, but the cause is what we wish to know in this particular case.

GRANULOSIS RUBRA NASI. Presented by DR. OLIVER and DR. FINNERUD.

A boy, aged 8, presented himself at the Children's Memorial Hospital because of redness and breaking out of the nose of more than seven years' duration. The disorder began during an attack of eczema of the face, which persisted for six months. He complained of periodic itching limited to the nose and wished treatment because all the boys called him "cherry-nose." His mother stated that the boy's face, and especially the nose, was usually covered with

perspiration, even when his body felt cold. The whole body perspired freely on the slightest exertion, but the face did so even in the absence of exertion and when the patient was at rest in a room of normal temperature.

Examination showed redness limited to the nose. This discoloration was made up of erythematous macules and papules varying in size from that of a pinpoint to that of a pinhead. All the red color disappeared on pressure. The nose was colder than the skin of the face and was stippled with minute beads of perspiration. The forehead and face elsewhere was also perspiring freely. The palms were moist, but not cold.

At the time of demonstration the patient had two red, pea-sized nodules on the left side of the nose. The mother stated that such nodules had never occurred before and had been present for two or three weeks. The patient had refused to permit aspiration of the nodules.

DISCUSSION

DR. MITCHELL: I saw a case over a year ago that was much like this, and from the therapeutic standpoint, roentgenotherapy was effective. The condition cleared up under this treatment. It seemed to be in that case, as Darier maintains, that the changes of the skin were due to the localized hyperidrosis. This child had marked hyperidrosis on the right side of the nose. I was surprised at the rapidity with which the condition cleared up in the case in which I administered treatment, but it had all the characteristics of, and apparently was, a case of granulosis rubra nasi.

DR. ZWICK: Jadassohn described occasional involvement of the median portion of the forehead and noted the familial occurrence of the condition which, according to the statement of the person accompanying the patient, is also the case here.

DR. FINNERUD: Since seeing this case I have looked up the literature on granulosis rubra nasi and have learned that the associated hyperidrosis of the forehead and face is not an uncommon symptom. Also, that the disorder, almost without exception, disappears about the age of puberty.

PITYRIASIS RUBRA PILARIS. Presented by DR. OLIVER and DR. FINNERUD.

A girl, aged 6, of fair general health, had had a generalized eruption of three months' duration. At the time of the first examination the eruption had been present for five weeks; the appearance had remained practically unchanged since that time. It began as a burning sensation of the soles which almost immediately followed stepping into a vat of freshly prepared mortar, and the mother believed it to be a "mortar burn." The skin of the soles became red, dry and cracked and within a few days the palms presented a somewhat similar appearance. Redness and roughness of the skin was next noticed on the back of the neck, on the extensor surfaces of the elbows and knees, and finally on all other areas.

The patient had had a gastro-intestinal disturbance for one month at the age of 2 years, and measles a few months later. She had a younger brother and sister, both living and well. The family history did not present any evidence of tuberculosis or other noteworthy disorders.

Examination revealed marked, diffuse hyperkeratosis of the palms and soles with fissuring, infiltrated erythematous plaques of the extensor surface in the vicinity of the elbows and knees, an erythematous seborrheic mask of the face and scalp, and a lichenoid eruption of general distribution which was most marked on the back of the neck. Roentgen-ray examination of the chest showed the following: "The lung shadows are increased in all lobes on the right side. The same shadows on the left of the apices are clear. These shadows resemble those of some previous lung pathology rather than active. There is no radiographic evidence of pulmonary tuberculosis at this examination." The Pirquet test was performed, but the patient did not return for the reading.

DISCUSSION

DR. HARRY R. FOERSTER: I agree with the diagnosis.

DR. FINNERUD: I think the interesting thing about this case is the fact that the lesions developed following exposure to external irritants. We had a patient at the Central Free Dispensary with a similar history; the mother stated that the disorder occurred following an attack of poison ivy dermatitis. I think Dr. Mitchell saw a case with Dr. Ormsby, which in the beginning resembled dermatitis venenata, but later developed into typical pityriasis rubra pilaris.

SCLERODERMA ON ABDOMEN. Presented by DR. MITCHELL.

A woman, aged 29, stated that lesions first appeared in July, 1923, on the abdomen, at which time she was told that she had a cancer of the skin. Two extensive dissections were performed at different times and the lesions were now recurring. Recently the patient had been told that her life depended on an immediate operation.

A linear, semicircular scar resulting from an incision extended entirely across the abdomen with the umbilicus in the concavity. From a point to the right of the umbilicus three parallel scars extended to the pubis. In the region of the umbilicus and about the intersection of the scars the tissue was hard, yellowish and of a waxy hue. Clinically and histologically, the tissue was sclerodermatous.

DISCUSSION

DR. WILE: It is interesting to note how a surgeon could be so mistaken in the diagnosis as to attempt excision.

DR. MITCHELL: There is no question about the diagnosis in this case. I have a section and it is unquestionably scleroderma. One can understand how a surgeon might assume that it was cancer en cuirasse because of the hardness. The interesting thing was that the girl had been badly frightened and had sought other advice before further operation. Her surgeon had told her that if she was not operated on at once she would die. Her general health is excellent and her basal metabolism — 10.

CASE FOR DIAGNOSIS. Presented by DR. ZEISLER.

A married woman, aged 48, presented lesions which had been present around the lips and under the surface of the nose since January, 1927. At that time she had had a severe case of pleuropneumonia, with what appeared to be herpes of the lips. The present lesions developed at the site of the herpes.

The lesions were round, dull red, firm nodules, and were not ulcerated. Diascopic examination did not reveal any nodules. The Wassermann reaction was negative.

Cautery had been used recently on the lesion on the lower lip and there was a superficial ulceration. Biopsy had not been permitted.

DISCUSSION

DR. WILE: I thought the case was one of noncaseating tuberculosis of the nose. I was struck by the fact that the healed lesion on the lip, on blanching it, closely resembled a superficial type of epithelioma. I think the lesion on the ala was typical of a so-called sarcoid.

DR. O'LEARY: A diagnosis of lupus vulgaris of the superficial type seems the most plausible to me. Under glass pressure definite nodules the color of apple-jelly are elicited.

DR. ZWICK: The case impressed me as one of lupus vulgaris tumidus, as a rapid diascopic examination indicated in the ischemic tissues the presence of, what I believe to be, apply-jelly nodules.

DR. ZEISLER: I had thought of either a true lupus vulgaris or sarcoid of the tuberculous type. I am sorry that I was not able to make a biopsy report.

SYPHILODERM OF UNUSUAL DISTRIBUTION. Presented by DR. EBERT.

A woman, aged 20, stated that seven months before presentation she developed two dozen or more small pustules on the body, face and extremities. After they had dried there were red spots which gradually increased in size until they reached their present dimensions. None of the spots had disappeared. There was no history of preceding lesions of the skin or mucous membrane. The patient said that she had been married three years before consulting me and had separated from her husband two years later. She had never been pregnant. She gave a history of kidney trouble of several years' duration and one year ago was under treatment at the Cook County Hospital for this condition. She had complained of weakness, night sweats and fever intermittently during the past three years. On Sept. 24, 1927, when she was first seen, the Wassermann reaction on the blood serum was negative.

When first seen there were two dozen or more coin-sized plaques with raised, nodular, somewhat scaly borders and depressed, dull red, slightly atrophic centers. The margins of many of these lesions were somewhat scalloped. The nodules varied in size from that of a pinhead to that of a matchhead and were of a brownish color under the diascope. At the right ala of the nose there was a punched-out, crusted ulcer about the size of a small matchhead. She was given a saturated solution of potassium iodide and on her return two weeks later the lesions had markedly improved. The discoloration remained unchanged and the atrophy was more marked. The nodules had been practically absorbed.

The Wassermann reaction of the blood serum after the iodide treatment was strongly positive.

DISCUSSION

DR. EBERT: This patient was first seen about two weeks before this meeting. The lesions at that time were definitely raised nodules which under the diascope showed a brownish color. At that time the blood Wassermann reaction was negative. She was given a short course of potassium iodide and the result was magical. The Wassermann reaction is now positive, but only relics of the eruption remain.

PARAFFINOMA. Presented by DR. EBERT.

A woman, aged 47, had gradually developed a painless tumor of the nose during the past three years. Thirteen years before presentation she had developed several furuncles on the face and one on the nasal septum, which had resulted in a depression of the end of the nose. Paraffin was injected into this lesion once shortly after its development.

She was examined recently in the nose and throat department of the Central Free Dispensary. A perforation of the septum was found and nasal polypi which were removed.

Several Wassermann tests before and after provocative injections of neoarsphenamine had been negative.

Transversely across the nose at the junction of the bone and the cartilage, there was a raised, moderately infiltrated tumor involving the skin and subcutaneous tissue. The skin over it was unchanged and of a yellowish-brown tint.

STOMATITIS (BISMUTH). Presented by DR. EBERT.

A Mexican woman, aged 35, first appeared at the Central Free Dispensary in November, 1926, with an extensive ulcerating, nodular, syphiloderm of the lower lip and chin. The Wassermann reaction was strongly positive on the blood serum. She was given a regular course of treatment, consisting of six injections of neoarsphenamine and fifteen weekly intramuscular injections of 0.2 Gm., potassium bismuth tartrate.

Under this treatment the lesions of the skin cleared up rapidly. Treatments were not given from April 15 to July 6, 1927. At that time the Wassermann

reaction was still strongly positive and she was given five more injections of neoarsphenamine and twelve more injections of potassium bismuth tartrate. A severe gingivitis developed, followed by ulceration of the mucous membrane in the right buccal pouch. An intense blue line also developed along the gingival margins. She complained of pains of the bones and headache. She was treated at the Cook County Hospital and later at the Central Free Dispensary with daily intravenous injections of sodium thiosulphate. The condition had greatly improved.

At the time of presentation there were several bluish-black, raised patches on the buccal mucosa opposite the last molars, most marked on the right side. There was an intense blue line at the gingival margins, and punctate, bluish deposits on the papillae of the tongue, particularly on the right side.

DISCUSSION

DR. ZWICK: The localization of bismuth sulphide in the papillae of the tongue does not seem to be of frequent occurrence, unless it has been generally overlooked. I have never observed it, although the pigmentation in the margin of the gums is more common with bismuth than with mercury. Loehe has recently stated that the bismuth pigmentation of the gums is a relatively harmless occurrence, in contradistinction to the lingual localization which he looks on as a definite sign of bismuth intoxication.

DR. HEDGE: We have a good many cases of questionable stomatitis which prove to be nothing more than the pigmentation in the mouth of a colored person. We see many cases in which it is difficult to differentiate between the normal pigmentation and the discoloration which is due to the disease. I think that in colored patients the line of pigmentation is usually further away from the line of the teeth than is the case in mercury or bismuth pigmentation.

DR. EBERT: The case was shown primarily with the idea that it might stimulate some discussion regarding the frequency of bismuth stomatitis. This woman at one time was ill but the condition has all cleared up.

CASE FOR DIAGNOSIS. Presented by DR. SENEAR.

A girl, aged 20, for the past months had complained of a disorder of the finger-nails. History of a general disturbance was not elicited nor was there any eruption on the body. The nails were negative for fungi by direct examination and culture. Hyperkeratosis was not found on scraping the nail-bed and plate.

The nails of several fingers showed a separation of the nail plate from the bed, which on some of the fingers extended nearly half way back from the free margin.

DISCUSSION

DR. MITCHELL: The first thing I thought of was an early psoriatic change in the nails, and I think one should pay particular attention to the possible development of psoriasis in this case. The changes are not typical, but the condition on one border of the nails was suggestive. The patient said there had not been any lesions on the knees or elbows.

DR. FOERSTER: I agree with Dr. Mitchell as to the diagnosis in this case. I inquired particularly about manicuring, and the patient told me she has never been to a manicurist but attends to her nails herself. A corner of one of the nails is thickened, opaque and amber; several nails have shallow pits, and none have transverse furrows, which are points of importance for diagnosis.

DR. SENEAR: Dr. Cornbleet made cultures and they were negative.

LICHEN PLANUS. Presented by DR. FINK (by invitation).

An infant, aged 7 months, presented a linear lesion which traversed the left lower extremity posteriorly from the buttock to the heel, converging as it

approached the heel until it appeared as a slender band in that region. The mother stated that the lesion appeared at the age of about 5½ months and had progressed gradually downward. It was composed of closely aggregated, flat topped, shiny papules slightly elevated above the normal skin.

DISCUSSION

DR. O'LEARY: I was unable to confirm the diagnosis of lichen planus on this infant. The lesion appears to be that of a linear nevus and suggests the advisability of further observation to determine whether or not it is an ichthyosis hystrix.

DR. HARRY FOERSTER: I agree with Dr. O'Leary.

DR. FINNERUD: My impression was that the condition was a linear nevus.

DR. FINK: I cannot speak from experience, never having seen a similar case, but the lesion corresponded with the description of lichen planus linearis. Since the prevailing opinion is that it is a nevus I feel that I should use roentgenotherapy and, if the lesion responds, it may satisfy me as does the diagnosis. If I can secure a biopsy I will report at a future meeting.

CASE FOR DIAGNOSIS. Presented by DR. OLIVER and DR. FINNERUD.

A Polish girl, aged 8, had a slightly itching eruption of the face, neck, upper chest, buttocks, back of thighs, forearms, hands, knees and sides and back of ankles which had been present since she was 7 months old. The eruption was most marked over the knees, elbows, finger joints and face; the trunk and scalp were practically free. The mother stated that the eruption began as a redness and peeling of the face, hands and feet and that almost from the beginning the skin had been shiny and shrivelled and of its present appearance. She also stated that the child's skin had always bruised and sunburned easily and for this reason she had been careful to keep the child out of the sun. For six months the child had been getting weaker, and had lost about 5 pounds (2.3 Kg.) in the past year. The child was born full term and the delivery was normal. She walked at 9 months, talked at 1½ years and dentition began at 3 months. She was breast fed until 9 months old, the condition of the skin having developed while she was still on the breast. Strabismus had been present since the age of 1 year. Her appetite had always been rather poor, but her bowels had been regular. Micturition had been unusually frequent since birth. The father and mother were living and well, as were three other children, none of whom had had a skin disorder. The family history did not present any evidence of tuberculosis or other noteworthy disorders. Although the child had always been rather undernourished, her only previous disorders were measles and whooping cough.

Examination revealed bluish red, shiny areas of telangiectasia varying in size from that of a finger-nail to that of a palm; there was atrophy in the foregoing regions. The eruption was perfectly symmetrical. The entire face was involved and follicular hyperkeratosis was most marked on the forehead. The scalp was normal aside from some dry scaling. Many of the teeth were carious and the gums were red. The patient held the mouth open, apparently habitually. Aside from the strabismus, noteworthy changes were not found in the eyes. The pharynx and tonsils were red and swollen, and numerous cervical lymph glands were palpable. The heart and lungs were normal, but the thorax was poorly developed. Physical examination did not reveal any abnormality of the abdomen or genitalia, aside from the fact that the musculature of the abdomen and extremities was poor. The reflexes, superficial and deep, were normal. Diphtheria bacilli were not revealed in cultures of the nose and throat and the vaginal smear did not reveal gonococci. The Pirquet test was normal with reading at twenty-four, forty-eight and seventy-two hours. The blood chemistry was normal and the blood Wassermann, Kolmer, and Kahn tests were negative. Urinalysis was normal and the blood observations

were as follows: red blood cells, 4,200,000; white blood cells, 5,400; hemoglobin, 80 per cent; polymorphonuclears, 59 per cent; small and large lymphocytes, 39 per cent; eosinophils, 1 per cent; and transitional cells, 1 per cent. The basal metabolic rate in the Benedict Talbot standard reading was 1.6 per cent above normal. During observation over a period of two weeks in the hospital the patient's respiration averaged 25, the pulse rate 100, and the body temperature, 99.2 F. The lowest body temperature recorded was 98.6 and the greatest rise in temperature was reached each day at 4 o'clock in the afternoon.

Histologic section from a patch of the left forearm showed atrophy of the epidermis, a thinned, but not definitely sclerotic, corium and slight vascular dilation. The section studied did not contain any hair follicles or sebaceous glands and only remnants of one sweat gland.

DISCUSSION

DR. ZEISLER: I would suggest acrodermatitis chronica atrophicans as the diagnosis.

DR. WILE: I think this is the most interesting case that has been presented and I do not think that the picture in this case agrees with any known entity. I believe there are three things to consider: (1) poikiloderma chronica atrophicans; (2) scleroderma, and (3) acrodermatitis chronica atrophicans. Of these three I think the most likely is scleroderma. There was a peculiar silvery atrophy which is seen in some forms of scleroderma. I think the diagnosis of an unusual form of scleroderma fits better than anything else.

DR. PUSEY: In general, I feel as Dr. Wile does. I thought of poikiloderma and diffuse scleroderma and then of acrodermatitis. I think acrodermatitis can be excluded. I have not seen enough poikiloderma to discuss it intelligently, but am inclined to believe the case can be accepted as a diffuse scleroderma, with extreme compensatory vascular changes.

DR. MICHELSON: The child appears to be distinctly below par mentally and physically. I think the case is one of scleroderma, and believe that every investigation possible should be made to rule out any endocrine disturbance.

DR. O'LEARY: In my differential diagnosis I thought of an acrodermatitis chronica atrophicans, poikiloderma atrophicans vasculare and scleroderma. The diagnosis of scleroderma seemed the least probable to me. There was no scleroderma to be noted outside of the atrophic patches. In a child of this age one would not expect scleroderma to become atrophic so rapidly without some patches retaining the sclerodermatous characteristics. I confess I am not sufficiently familiar with the picture of poikiloderma to make such a diagnosis, but the pronounced atrophy with the erythema apparently preceding the atrophy of the extremities seems to me to warrant a diagnosis of acrodermatitis chronica atrophicans. Dr. Wise called attention recently to the fact, with which I am in accord, that there is no relationship between acrodermatitis chronica atrophicans and scleroderma. In my experience, atrophy other than of the finger tips is a rare observation in cases of scleroderma, and, as this child shows patches of atrophy unassociated with scleroderma, it is difficult for me to classify it in any but the idiopathic atrophy group. Scleroderma is a sclerosing disease of which this child does not show any evidence, while acrodermatitis chronica atrophicans is an atrophic disease and I am sure we agree that this child shows definite plaques of atrophy.

DR. ZWICK: Although the descriptive adjectives, atrophicans reticulare applied to Jacobi's poikiloderma most nearly describe the picture as it is presented, I was so impressed by the statements of the person accompanying the patient, that exposure to sunlight first started and now exacerbates the condition of the skin, that I am inclined to think that Kaposi's xeroderma pigmentosum is within the range of diagnostic possibilities and will have to be ruled by the factor of time, i. e., by the further development of the case.

DR. FOERSTER: I agree with Dr. Wile and Dr. Pusey and call attention particularly to both forearms where the skin is peculiarly fixed and glossy, and the musculature appears to be contractured, giving the arm a peculiar spindle shape. The face is masklike, dirty gray, and the forehead remains smooth when the girl looks up. It is conceivable that an early stage of edema or induration, though present, was of such moderate development that it passed unnoticed, and that since its inception the disorder has progressed in a relatively mild form.

DR. ZEISLER: I should like to know whether there is any interference with the mobility of the joints in this case. In all the extensive cases of scleroderma that I have seen this has been present.

DR. PUSEY: It seems to me that on the forearms the skin was tense and the whole thing had a suggestion of scleroderma and not the soft feeling of acrodermatitis. The face seemed to lack the line of expression and to have the fixed, somewhat superficial stare that occurs in cases of scleroderma.

DR. OLIVER: I am glad the case has stimulated so much discussion. When we first saw this child we thought possibly it was a case of poikiloderma. I read over Dr. John Lane's article, in which all the published cases of poikiloderma are abstracted, and felt at first that the child was too young to have this disorder, but there are several cases reported in children as young as this. I think in every case that has been presented before the different societies there has been just as much discussion as to whether the condition was poikiloderma or scleroderma.

DR. FINNERUD: We have had this child in the hospital for two or three weeks and have worked the case up as thoroughly as we could. We have considered this poikiloderma and scleroderma on alternating weeks, but have hardly considered acrodermatitis chronica atrophicans. The basal metabolic rate by the Benedict Talbot standard is 1.6 per cent above normal. The cases of poikiloderma reported in children, the youngest of whom was 6 at the time of onset, are practically identical with this case, and, it seems to me, it is possible that those cases stood as good a chance of being scleroderma as this. Evidently the basal metabolic rate is considered the most important point in the differential diagnosis.

ANGIOKERATOMA OF SCROTUM. Presented by DR. STILLIANS.

A man, aged 37, American, a draftsman, stated that red lines and warts appeared on the scrotum nine years prior to presentation and had progressed since that time.

Many minute, dark red papules, varying from 0.5 to 3.0 mm. in diameter, were seen along dilated venules. Several of the largest had been removed by fulguration.

DISCUSSION

DR. WILE: I do not agree with the diagnosis. I have had occasion recently to review the whole subject of angiokeratoma and am convinced that a large group of cases is placed with the angiokeratomas which do not belong there, particularly this type of case. The essential features of true angiokeratoma are the occurrence of angiomatous or hemorrhagic lesions, which rapidly become verrucous, infected, and then leave atrophy. They occur particularly over bony prominences, such as over the fingers, ankles, knees and elbows. In other words, they occur at points of pressure. These cases are rare. The cases that occur on the scrotum, which have been called angiokeratoma, are, I think, common, and are really not more than angiomatous lesions, exactly as one finds them late in life all over the body. They have none of the vegetative verrucous features of true angiokeratoma.

DR. MITCHELL: Heretofore I have not considered this type of lesion as angiokeratoma. I have seen two similar cases recently which I assumed to be simple angioma.

DR. PUSEY: I was much interested in Dr. Wile's discussion. I have been accepting some of these cases as Mibelli's disease. They are sometimes a little bit warty. I am perfectly willing to accept Dr. Wile's point against Mibelli's disease in this case. I think that the lesions are small angiomas occurring on the scrotum, a condition which is not at all uncommon.

DR. WILE: In regard to just where angiokeratoma belongs in classification, it would seem that it has many points of resemblance with epidermolysis bullosa of the acquired type. Trauma seems to be a factor in the occurrence of the lesions, and an occasional microscopic observation of the loss of elastica has been noted in angiokeratoma, as in epidermolysis bullosa. Atrophy is a striking feature of the cases and is not found in the scrotal form of angioma.

DR. ZWICK: Angiokeratomas on the scrotum would be noted more often, possibly, if a systematic search were made for it. In some patients similar lesions occur also on the chest. Whereas the majority of authors look on them as inflammatory, others classify the angiokeratomas among the nevi vasculares tardivi. The first belong to the type described by Mibelli. In regard to the second the question arises, whether there is any relation between it and the "senile" angiomas (called "points rubis" by the French) so frequently seen on the trunk and extremities of persons over 40 years of age.

DR. STILLIAN: I am glad to have the information given us by Dr. Wile.

PITTSBURGH DERMATOLOGICAL SOCIETY

Regular Meeting, Oct. 20, 1927

L. G. BEINHAUER, M.D., *Chairman, Presiding*

HYDROA VACCINIFORME. Presented by DR. GUY and DR. JACOB.

A girl, aged 9 years, presented discrete vesicles the size of a pea on the arms, face and ears, some of which resulted in scar formation. Attacks occurred in the spring and fall.

A CASE FOR DIAGNOSIS. Presented by DR. PHILLIPS.

E. R., a barber, aged 40, presented a lesion on the left side of abdomen about 3 inches (7.6 cm.) in diameter. It consisted of a somewhat reniform arrangement of ulcers which had coalesced in several places. The ulceration extended through the skin and into the subcutaneous tissues, was sharply marginated, and contained but little pus. It had started to ulcerate three years prior to presentation. Previously there had been a pea-sized tumor at the site of the present ulceration; the first ulcer developed on this red tumor mass and ulcerated it away. Unfiltered roentgen-ray was used and the area was healed, with the exception of a necrotic area in the center about 1 inch (2.5 cm.) in diameter which was excised and a skin graft performed. This area has remained healed, but other ulcers developed at the edge and have resisted all efforts to heal. The blood Wassermann was negative as was the therapeutic test with neoarsphenamine and mixed treatment.

The specimen was roughly circular in size and about 4 cm. in diameter. It consisted of skin and subcutaneous tissue. The skin was apparently very thin and was covered by a light brown crust. The subcutantous tissue was fairly dense on palpation as if from a proliferation of fibrous tissue. There was not any evidence of extension of the process into or through the subcutaneous tissue.

Microscopically, the specimen was composed of dense fibrous tissue into which sheets and cords of epithelial cells were infiltrating. These cells varied greatly in size, shape and staining.

A diagnosis of prickle cell epithelioma of the wall of the left side of the chest was made.

NOTE: The section which has been described was cut from the subcutaneous tissue and gave evidence that infiltration of the malignant cells was more wide spread than was realized at first from the study of the quick section.

DISCUSSION

DR. HOLLANDER: I think that it would be unwise to express a definite opinion as to the diagnosis of the case at this late date as the previous treatments, roentgen-ray and excision followed by skin grafting changed the picture sufficiently to enable one to come to a definite conclusion.

CASE FOR DIAGNOSIS AND TREATMENT. Presented by DR. H. G. WERTHEIMER.

S. M., a woman, aged 35, born in Czecko-Slovakia, first came to the medical clinic, Feb. 11, 1927. She complained of dyspnea, pain in the chest and presented swelling and redness of the distal phalanges of the fingers of the left hand and of three fingers of the right hand. On the palmar aspect of the thumbs at the distal end was a hard, noninflammatory growth.

The patient said that she first noted the swelling of the ends of her fingers two years previously, and that they were not painful at that time. Recently they had become painful. Nine years previously the patient had had her appendix removed while pregnant and soon after this she had developed "heart trouble." She had dyspnea; the swelling of the ankles and the fingers became progressively worse.

The patient had a normal blood count and the analysis of the urine was negative. The Wassermann blood test was negative. A roentgenogram of the distal phalanges of the fingers showed some decalcified areas, but there was not any evidence of hyperplasia of the bone. The medical department referred the case to the department of dermatology because they did not think that the swelling of the fingers was characteristic of pulmonary or cardiac osteo-arthropathy. At the time of her second visit to the clinic the patient presented a fluctuating inflammatory papule on the dorsum of the distal phalanx of the small finger of the right hand. This was aspirated and a smear made but a growth was not obtained.

Constant dressings of boric acid and magnesium sulphate were ordered. Potassium iodide was given internally. Filtered doses of roentgen-ray were given. No change has taken place. The patient is presented for diagnosis and suggestions for treatment.

DISCUSSION

DR. NORRIS: The questions in my mind were immediately cleared on the suggestion by Dr. Beinhauer of xanthoma tuberosum multiplex.

DR. PHILLIPS: I think that the condition is xanthoma tuberosum multiplex in an unusual location. I recently saw a similar case, but the lesions were all much smaller.

LICHEN PLANUS ANNULARIS HYPERTROPHICUS. Presented by DR. HOLLANDER and DR. BAER.

A. D., a colored boy, aged 12, presented a fairly generalized eruption affecting principally the lower extremities and occurring in patches over the entire body with the exception of the face and neck. The lesions are papular in character, occurring in round or oval patches causing hypertrophied areas. The pigmentary change was marked, as practically all the lesions looked black, especially in the center. Several lesions on the body and on the arms showed an hypertrophy around the edges and minute atrophy in the center, with this black pigment previously mentioned. On the arms, however, individual lesions could be found which were papular and had the typical lichen shine. Posteriorly,

except in the popliteal space, the body and legs are entirely clear from the lesions. A distinctly linear lesion was seen on the extensor surface of the left arm, the papules of which had faded out leaving a definite line of pigmentation.

The case was of interest as lichen planus hypertrophicus is rarely seen in children.

EPITHELIOMA OF THE SCALP. Presented by DR. SCHWARTZ and DR. BUSMAN.

A. C., a woman, married, aged 67, presented an almost palm-sized plaque of alopecia, scarring and ulceration of the upper part of her scalp. The lesion was irregular in outline, and showed a definitely raised pearly border especially along the lower side. There were numerous small pea-sized areas of ulceration with considerable adjacent scar tissue.

The patient was entirely deaf and her memory was poor. She contended that she had had some sort of a lesion in the scalp since about 3 years of age. The onset of the ulceration and activity was rather uncertain. A Wassermann test or biopsy had not been performed.

DISCUSSION

DR. NORRIS: The lesion is unusual in its location, but clinically, I agree with the diagnosis because of the definite evidence of a raised pearly border.

DR. PHILLIPS: If it were not for the distinct "pearly" border, a clinical diagnosis of a lesion of this type and location would be difficult. I also agree with the diagnosis in this case.

DR. BUSMAN: This lesion is a good example of what we mean by a "pearly" border. With a diagnostic feature as clear as this, a diagnosis should have been made previously and the patient treated. This case is another example of allowing an easily treatable lesion to progress from infancy until it becomes a real therapeutic problem both as to immediate eradication and chances of recurrence.

A CASE FOR DIAGNOSIS. Presented by DR. GUY and DR. JACOB.

A girl, aged 3, presented a palm-sized mass of two months' duration involving the right buttock. The condition began with severe pain in the buttock followed by the appearance of a "boil" that was drained by a physician and which did not heal. The mass was elevated from one-quarter to one-half inch; was sharply marginated and had a glazed, mucopurulent, secreting surface. Three days before presentation a similar lesion the size of a dime appeared in the right cubital space. The mucous membranes of the mouth were involved by white sodden plaques resembling mucous patches. A moderate leukocytosis was present and the patient ran a moderate low grade temperature. The section (presented) revealed a subacute inflammatory tissue with numerous polymorphonuclear cells, there being a few giant cells, but the bulk of the infiltration comprised round cells and leukocytes. The Wassermann test was negative.

DISCUSSION

DR. PHILLIPS: If these lesions were in an adult, the most probable clinical diagnosis would be granulome inguinale tropicum.

DR. BUSMAN: If I were to commit myself on a clinical diagnosis I would say tuberculosis. The lesion has the smooth, moth eaten base, the undermined border and a serosanguineous discharge. The child appears greatly below par physically and is a good subject for tuberculosis. The temperature is not as high as one would expect with such a virulent local streptococcus or staphylococcus infection, nor does she have the typical temperature curve of an infection of the blood stream.

SENILE KERATOSES MULTIPLE EPITHELIOMATA. Presented by DR. SCHWARTZ and DR. BUSMAN.

A. McC., aged 55, a housewife, presented a pea-sized, elevated, glistening, pearly, telangiectatic, hard, fibrous, nonulcerating lesion of the right side of the nose; a small similar lesion below a soft fibrous nevus on the right side of the neck; a flat, crusted, centrally ulcerated, dime-sized lesion with a pearly fibrous border of the right side of the neck; a small scaly, slightly pearly, bordered lesion of the right side of the chin, and left side of the temple and two similar lesions behind the left ear. There was a large raised verrucous lesion over the right clavicle and several similar precancerous lesions of the face and neck. There was a moderate sized, port-wine stained, flat nevus at the outer canthus of the right eye. There was a flat, noncontractile scar, 1 inch in diameter on the right cheek where a similar lesion had been removed by roentgen ray seven years previously. The lesions in general were interesting in that the patient showed all stages of lesions from an early senile keratosis to the raised pearly and flat ulcerating type of epithelioma.

DISCUSSION

DR. PHILLIPS: This is the type of case that should be repeatedly shown to general practitioners. These lesions should be recognized early and destroyed, as emphasized by Dr. McKee at our recent meeting. The patients should be kept under frequent observation. I have a patient now who has hundreds of the seborrheic type of keratoses on the back and I am debating as to the best type of procedure on account of the great number of lesions.

DR. FISCUS: I feel as Dr Phillips does, that these cases should be shown often. They are easily diagnosed and treatment should be begun early and the patient kept under observation.

DR. BUSMAN: The clean scar on the cheek where a similar lesion was removed seven years previously shows how amenable the lesions are to treatment.

ACRODERMATITIS CHRONICA ATROPHICANS AND SCLERODERMA. Presented by DR. HOLLANDER and DR. GOLDMANN.

E. A., aged 49, a Jewish housewife, presented a bilateral atrophy of the skin which involved the lower extremities. The condition was somewhat variable in appearance, at different levels. Over the dorsum of the foot it was hard and board-like, occurring in the form of a band; over the skin of the rest of the extremities it was thin and reticular, showing a little erythema and fine scaling; over the tibia there appeared occlusion of the superficial veins. There were pigmentary changes of brownish-yellow patches, and also areas of depigmentation present. The posterior aspect of both legs was reddened and showed the presence of a dermatitis. Over the hips there were striated areas of bands present, resembling a scleroderma, and having the infiltration of a scleroderma. The finger tips were somewhat reddened, although there was no acromosis present, and there was apparently a stiffening present at the tips. Outside of this the skin appeared to be fairly moist and in fair condition. The condition was of about nine years' duration and was progressive; there was some itching present.

DISCUSSION

DR. NORRIS: This case is interesting and shows clearly the atrophy, the fine tufts of vessels and the sclerodermatous infiltration.

DR. BUSMAN: This case certainly is primarily one of scleroderma.

DR. GUY: It is not unusual to see the two conditions together.

DR. HOLLANDER: The patient was presented because some of the clinical features of the disease were well marked. The atrophy of all the layers of the skin with the resultant appearance of the blood vessels, the cigaret-paper like atrophy about the knees and the hard band like areas of scleroderma about the thighs were marked. The patient will be given sodium thiosulphate intravenously and by mouth to see whether the course of the atrophy can be stopped.

TUBERCULOUS ULCER OF THE TONGUE. Presented by DR. GUY and DR. JACOB.

A man, aged 30, presented a lesion of the tongue of six months' duration. The dorsal surface at the junction of the anterior and middle third was involved by an irregular quarter-size ulceration which was papillomatous at the center, deeply fissured and painful. The patient also had a tuberculous laryngitis and pulmonary tuberculosis.

LYMPHANGIOMATA (ACQUIRED). Presented by DR. SCHWARTZ and DR. BUSMAN.

T. N., a Syrian peddler, married, aged 42, presented a cauliflower-like mass involving the entire scrotum and right groin. The individual lesions, pinkish-white nodules, varied in size from that of a pinhead to that of an olive and were filled with a milky white serum which exuded freely on pressure. There were also several transparent vesicles on the penile shaft and the right leg which varied in size from that of a pinhead to that of a pea. There was an operative scar in both groins, the result of an herniotomy in 1908. There was an appreciable elephantiasis of the right leg. The condition started soon after operation in 1908. There was continual drainage and the leg soon began to enlarge. The cauliflower-like lesions developed about three and a half years previously. The patient's general health was good. Neurologic examination was essentially negative. The urinalysis was negative. The blood pressure was 110 systolic and 60 diastolic. The spinal fluid, blood Wassermann and serologic tests were negative.

DISCUSSION

DR. AMSHELL: I saw a case similar to this in a young Jewish man presented before the New York Academy of Medicine and the Manhattan Dermatological Society. Several biopsies were taken and showed nothing but a granulomatous tissue. A diagnosis of lymphogranulomatosis of unknown origin was made.

G. J. BUSMAN, Secretary.

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DERMATOLOGY

Adenitis of Scarlet Fever in Children. Nobécourt, Progrès méd. **53**:1570 (Oct. 8) 1927.

Alder Wood Dermatitis. S. Brügel and A. Perutz, Arch. f. Dermat. u. Syph. **153**:661 (Oct. 23) 1927.

Alkali Treatment in Diphtheria and Scarlet Fever. B. A. Peters, Lancet **2**:1231 (Dec. 10) 1927.

Association of Measles and Diphtheria. P. Joannon, Progrès méd. **53**:1610 (Oct. 15) 1927.

Atypical Erysipelas and Pregnancy. H. Siegmund, Zentralbl. f. Gynäk. **51**:2787 (Oct. 29) 1927.

Benzocaine-Chaulmoogra Oil in Treatment of Leprosy. F. A. Johansen, Pub. Health Rep. **42**:3005 (Dec. 9) 1927.

Blue Nevus. C. Kreibich, Arch. f. Dermat. u. Syph. **153**:804 (Oct. 23) 1927.

Brooke's Epithelioma Adenoides Cysticum. L. N. Maschkillejsson, Arch. f. Dermat. u. Syph. **153**:721 (Oct. 23) 1927.

Bullous Impetigo Complicating Varicella. L. A. Eldridge, Jr., and T. M. Rivers, Bull. Johns Hopkins Hosp. **41**:354 (Dec.) 1927.

Capillary Figures on Margins of Necrotic Areas. S. Bettmann, Arch. f. Dermat. u. Syph. **153**:574 (Oct. 23) 1927.

Carcinoma in Leprosy. W. Kobayashi, Acta derm. **10**:441 (Oct.) 1927.

Certain Effects Produced by Shock and Death on Vessels of Skin. H. B. A. R. Densham and H. M. Wells, Quart. J. Exper. Med. **18**:297 (Dec. 7) 1927.

Chemotherapy in Diseases of Skin. P. E. Bechet, New York State J. Med. **27**:1293 (Dec. 1) 1928.

Chronic Atrophic Dermatitis with Formation of Multiple Nodules and Cords. E. Delbanco, A. Lippmann and P. Unna, Jr., Arch. f. Dermat. u. Syph. **153**:706 (Oct. 23) 1927.

Classification of Parasitic Diptera Larvae in Human Skin and Eye. A. and M. Hobmaier, Deutsche med. Wchnschr. **53**:1858 (Oct. 28) 1927.

Climatic Factors in Light Erythema and Pigmentation. R. Stahl and G. Simsch, Klin. Wchnschr. **6**:1984 (Oct. 15) 1927.

Cure of Condylomas by Suggestion. J. Bonjour, Schweiz. med. Wchnschr. **57**:980 (Oct. 8) 1927.

Dermatoglyphics in Jews. H. Cummins and C. Midlo, Am. J. Phys. Anthrop. **10**:91 (Jan.-March) 1927.

Dermatograms. S. Bettmann, Arch. f. Dermat. u. Syph. **153**:637 (Oct. 23) 1927.

Diagnosis of Scarlet Fever by Complement Deviation Reaction. L. Bethoux, J. de physiol. et de path. gén. **25**:553 (Sept.) 1927.

Diseases of Skin in Asthma. K. H. Baagöe, Acta med. Scandinav. **67**:189 (Nov. 22) 1927.

Early Diagnosis of Scarlet Fever. R. Rehsteiner, Schweiz. med. Wchnschr. **57**:981 (Oct. 8) 1927.

Effect of Circulation on Skin-Constrictor (Psychogalvanic) Reflex. H. B. A. R. Densham and H. M. Wells, Quart. J. Exper. Physiol. **18**:283 (Dec. 7) 1927.

Effect of Kala-Azar on Leprosy. E. Muir, Indian J. M. Research **15**:497 (Oct.) 1927.

Elastometry in Dermatology. F. Schmidt-Labaume, Arch. f. Dermat. u. Syph. **153**:564 and 766 (Oct. 23) 1927.

Epidemics of Infectious Exanthems of Indeterminate Nature. Boinet and J. Piéri, Presse méd. **35**:1345 (Nov. 5) 1927.

Epidermolysis Bullosa Hereditaria. Heymann, Arch. f. Dermat. u. Syph. **153**:624 (Oct. 23) 1927.

Erysipelas: Treatment. E. S. Platou, F. W. Schlutz and L. Collins, Am. J. Dis. Child. **34**:1030 (Dec.) 1927.

Essential Thrombocytopenic Purpura. B. G. Efron, New Orleans M. & S. J. **80**:391 (Dec.) 1927.

Etiology of Granuloma Annulare. O. Dittrich, Arch. f. Dermat. u. Syph. **153**: 599 (Oct. 23) 1927.

Etiology of Scarlet Fever. Mandelbaum, Müchen. med. Wchnschr. **74**:1903 (Nov. 11) 1927.

Exanthematic Typhus and Typhoid Infection with Exanthem. D. Olmer, and J. Olmer, Presse méd. **35**:1346 (Nov. 5) 1927.

Five Cases of Leprosy Treated with Javanin. F. Eubanas, J. Philippine Islands M. A. **7**:407 (Nov.) 1927.

Function of Subpapillary Vascular Plexus in Skin. E. Wollheim, Klin. Wchnschr. **6**:2134 (Nov. 5) 1927.

Furunculosis. P. J. Amaya, Repert. de med. y cirug. **18**:339 (April) 1927.

Hardness of Roentgen Rays in Relation to Erythema. P. Hess, Strahlentherapie **27**:146, 1927.

Herpes Zoster. G. Pieri, Arch. ital. di chir. **17**:545 (April) 1927.

Influence of Respiratory Movements on Cutaneous Circulation. R. J. Collier, H. B. A. R. Densham and H. M. Wells, Quart. J. Exper. Physiol. **18**:291 (Dec. 7) 1927.

Intradermal Reaction in Schistosomiasis. N. H. Fairley and F. E. Williams, M. J. Australia **2**:811 (Dec. 10) 1927.

Iodide Antimony Treatment of Leprosy. E. Muir, Indian J. M. Research **15**:507 (Oct.) 1927.

Iontophoretic Treatment of Alopecia. J. Sellei and J. Fenyö, Arch. f. Dermat. u. Syph. **153**:603 (Oct. 23) 1927.

Leprous Changes in Blood Vessels. H. P. Lie, Norsk. Mag. f. Lægevidensk. **88**:1108 (Nov.-Dec.) 1927.

Madura Foot. O. Da Fonseca, Jr., and A. E. De Arêa Leão, Sciencia méd. **5**:536 (Sept.) 1927.

Medicinal Skin Emboli. W. Freudenthal, Arch. f. Dermat. u. Syph. **153**:730 (Oct. 23) 1927.

Mucin in Skin Diseases. C. Kreibich, Arch. f. Dermat. u. Syph. **153**:799 (Oct. 23) 1927.

New Method for Skin-Grafting Mastoid Cavity and for Closing off Eustachian Tube at Its Tympanic End. A. Kahn, Laryngoscope **37**:889 (Dec.) 1927.

New Method of Covering Denuded Areas with Surrounding Skin. E. D. Highsmith, Surg. Gynec. Obst. **45**:823 (Dec.) 1927.

Pathology of Experimental Virus: Herpes Virus Encephalitis in Guinea-Pig. S. Flexner, J. Exper. Med. **47**:23 (Jan. 1) 1928.

Pellagra Among Alcoholic Addicts. J. V. Klauder and N. W. Winkelman, J. A. M. A. **90**:364 (Feb. 4) 1928.

Physical Agents in Dermatology. S. Barcat, Progrès méd. **53**:1663 (Oct. 22) 1927.

Physical Therapy in Diseases of Skin. C. E. Cook, Jr., J. Maine M. A. **18**:207 (Nov.) 1927.

Poikilodermia Atrophicans Vascularis with Unusual Findings. H. G. Rottmann, Arch. f. Dermat. u. Syph. **153**:747 (Oct. 23) 1927.

Pollen Allergy: Genesis of Skin Hypersensitiveness in Man. R. W. Lamson and H. Miller, Arch. Int. Med. **40**:618 (Nov.) 1927.

Progress of Treatment in Culion Leper Colony to March, 1927. B. de Vera, J. Philippine Islands M. A. **7**:361 (Oct.) 1927.

Relation Between Skin and Vitamins. W. Richter, Arch. f. Dermat. u. Syph. **153**:697 (Oct. 23) 1927.

Response of Allergic and Nonallergic Skin to Inflammatory Chemical and Physical Irritations, E. Rajka and K. Pogány, Arch. f. Dermat. u. Syph. **153**:615 (Oct. 23) 1927.

Rôle of Finger Nails in Mechanism of Infection with Anthrax. H. Lindtrop, Arch. f. Dermat. u. Syph. **153**:793 (Oct. 23) 1927.

Rôle of Skin in Production of Antibodies, of Anaphylaxis and of Anti-anaphylaxis. E. Klukhine, Ann. de l'Inst. Pasteur **41**:1108 (Oct.) 1927.

Scarlet Fever: Relation Between Antitoxin in Blood and Skin Sensitivity to Toxin in New-Born Infants and in Their Mothers. J. V. Cooke, H. R. Keith and L. Ermatinger, Am. J. Dis. Child. **34**:969 (Dec.) 1927.

Serum Prophylaxis of Measles. A. N. Kingsbury and M. Watson, J. Hyg. **27**:1 (Nov.) 1927.

Serum Treatment of Scarlet Fever. B. Mendes, Rev. de méd. **12**:324 (July) 1927.

Skin Diseases in Disturbances of Ovarian Function. O. Herschan, München. med. Wchnschr. **74**:1756 (Oct. 14) 1927.

Skin Reactions in Asthma. A. Anthony, Klin. Wchnschr. **6**:2141 (Nov. 5) 1927.

Skin Tuberculosis and Immunity of Organism. F. von Poór, Arch. f. Dermat. u. Syph. **153**:692 (Oct. 23) 1927.

Sodium Hydnocarpate in Leprosy: Improvements in Administration. E. Muir, Indian J. M. Research **15**:501 (Oct.) 1927.

Specific Skin Reactions in Allergic Infections. M. Juon, Schweiz. med. Wchnschr. **57**:1031 (Oct. 22) 1927.

Subcutaneous Correction of Hump Nose. E. Eitner, Wien. klin. Wchnschr. **40**:1449 (Nov. 17) 1927.

Suppurating Dermoid of Cerebellum: Case. J. Todesco, Lancet **2**:1340 (Dec. 24) 1927.

Tattooing and Methods of Its Removal. Marvin D. Shie, J. A. M. A. **90**:94 (Jan. 14) 1928.

Tertiary Manifestations of Yaws in Nose and Throat in Philippine Islands. C. N. Ayuyao, J. Philippine Islands M. A. **7**:411 (Nov.) 1927.

Tetanus Following Vaccination Against Smallpox. C. Armstrong, Pub. Health Rep. **42**:3061 (Dec. 16) 1927.

Thyroid and Skin Diseases. B. Sparacio, Arch. di pat. e clin. med. **6**:448 (Sept.) 1927.

Treatment of Erysipelas in Children. M. Giuffrè, Pediatria **35**:920 (Sept. 1) 1927.

Tuberculoid Leprosy. V. Klingmüller, Arch. f. Dermat. u. Syph. **153**:584 (Oct. 23) 1927.

Tuberculosis of Skin: Classification. F. B. Miller, Atlantic M. J. **31**:157 (Dec.) 1927.

Use of Leeches in Treatment of Phlebitis. A. Hamm and A. Schwartz, Schweiz. med. Wchnschr. **57**:1125 (Nov. 19) 1927.

Use of Supersoft Roentgen Rays (2 A) in Dermatology. J. J. Eller, Am. J. Roentgenol. **28**:433 (Nov.) 1927.

Varicella and Pemphigus. P. Lereboullet and M. David, Arch. de méd. d. enf. **30**:665 (Nov.) 1927.

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Acquired Syphilis of Intestines. K. Nishikawa, Arch. f. Dermat. u. Syph. **153**:539 (Oct. 23) 1927.

Amyotrophic Syphilitic Meningomyelitis: Two Cases with Argyll Robertson Pupils. T. T. Stone, J. Nerv. & Ment. Dis. **66**:595 (Dec.) 1927.

Analysis of Wassermann, Kahn and Meinicke Tests. F. R. Schmidt and R. C. Zickmann, Am. J. Syph. **11**:614 (Oct.) 1927.

Aortic Signs of Hereditary Syphilis in Child. J. Martagão Gesteira, Arch. de méd. d. enf. **30**:633 (Nov.) 1927.

Are We Dermatologists Syphilologists? J. L. Kirby-Smith, South. M. J. **21**:41 (Jan.) 1928.

Biochemistry of Wassermann Reaction. A. J. Hinkleman, Am. J. Syph. **11**:594 (Oct.) 1927.

Bismuth Salts in Treatment of Syphilis. G. Petges and O. Magimel, Liége méd. **20**:867 (Oct. 9) 1927.

Blood Changes in Bismuth Treatment of Syphilis. A. Herz, Wien. klin. Wchnschr. **40**:1350 (Oct. 27) 1927.

Bordet-Wassermann Reaction in Scarlet Fever. L. Béthoux, J. de physiol. et de path. gén. **25**:534 (Sept.) 1927.

Cardiac Syphilis (Syphilitic Aortitis). H. S. Martland, J. M. Soc. New Jersey **24**:689 (Dec.) 1927.

Case of Congenital Syphilis. J. R. McCord, Am. J. Syph. **11**:538 (Oct.) 1927.

Cerebral Antibodies in Syphilis Flocculation Experiments with Brain Extracts. F. Georgi and O. Fischer, Klin. Wchnschr. **6**:2031 (Oct. 22) 1927.

Chemical Analysis of Hypersensitiveness of Skin After Arsphenamine Dermatitis. W. Frei and R. L. Mayer, Arch. f. Dermat. u. Syph. **153**:606 (Oct. 23) 1927.

Chemical Constitution and Therapeutic Effect of Some Newer Antisyphilitic Remedies. G. W. Raiziss, Am. J. Syph. **11**:517 (Oct.) 1927.

Coincident Tuberculosis and Syphilis. C. O. Giese and B. E. McGovern, Colorado Med. **24**:367 (Dec.) 1927.

Experience with 2,000 Intramuscular Injections of Neoarsphenamine in Neurosyphilis. A. Gordon, Am. J. Syph. **11**:525 (Oct.) 1927.

Heart in Syphilitic Aortitis. B. J. Clawson and E. T. Bell, Arch. Path. **4**:922 (Dec.) 1927.

Joint Disease in Congenital Syphilis. A. Garretón Silva, Revista méd. de Chile **55**:456 (Oct.) 1927.

Malarial Treatment of General Paralysis. H. W. Bayly, Practitioner **119**:382 (Dec.) 1927.

Meinicke Syphilis Reactions. E. Meinicke, Deutsche med. Wchnschr. **53**:1764 (Oct. 14) 1927.

New Gold-Sol Reaction of Spinal Fluid. A. von Sarbó, Ztschr. f. d. ges. Neurol. u. Psychiat. **110**:549 (Sept. 10) 1927.

Nonspecific Wassermann and Agglutinin Reactions with Serums from Patients with Febrile Diseases. M. Corrigan, J. Infect. Dis. **41**:457 (Dec.) 1927.

Ocular Disease in Congenital Syphilis. G. Barmettler, Pediatria **35**:1224 (Nov. 15) 1927.

Pathogenesis of Metasyphilitic Diseases. E. Witebsky, München. med. Wchnschr. **74**:1914 (Nov. 11) 1927.

Pathology and Laboratory Diagnosis of Paresis. F. Proescher and A. Arkush, J. Nerv. & Ment. Dis. **67**:21 (Jan.) 1928.

Peritonitis in Tabes. C. Lagemann, Zentralbl. f. Chir. **54**:3278 (Dec. 17) 1927.

Preexisting Syphilis as Cause of Unresolved Pneumonia and Factor in Production of Postpneumonic Complication. J. B. Youmans and R. H. Kampmeier, Am. J. M. Sc. **174**:750 (Dec.) 1927.

Primary Syphilitic Lesions on the Skin of the Back in Rabbits. A. Groth and K. Arnold, München. med. Wchnschr. **74**:1881 (Nov. 4) 1927.

Rapid Simple Method for Simultaneous Titration of Amboceptor and Complement. J. H. Clark, Am. J. Syph. **11**:609 (Oct.) 1927.

Rôle of Syphilis in Etiology of So-Called Essential Epilepsy. L. Marchand and E. Bauer, Paris méd. **63**:294 (Oct. 15) 1927.

Simulation of Decerebrate Rigidity in Two Paretics. C. E. Kiely, Am. J. Syph. **11**:532 (Oct.) 1927.

Sulphur Treatment of Dementia Paralytica and Metasyphilis of Central Nervous Systems. K. Schroeder, Klin. Wchnschr. **6**:2189 (Nov. 12) 1927.

Surgical Syphilis of Kidney. S. A. Brofeldt, Acta Soc. med. Fennicae "Duodecim," Helsingfors, 1927, vol. 8.

Syphilis. W. Moser, Am. J. Syph. **11**:590 (Oct.) 1927.

Syphilis of Respiratory Tract. J. C. Navarro and E. A. Beretervide, Semana méd. **34**:1343 (Nov. 17) 1927.

Syphilis: Physical Examination in Diagnosis and Management. J. H. Stokes, J. M. Soc. New Jersey **24**:673 (Dec.) 1927.

Syphilis Resistant to Arsphenamine. E. Nathan, Klin. Wchnschr. **6**:2147 (Nov. 5) 1927.

Syphilis Resistant to Bismuth. I. C. Sutton, Am. J. Syph. **11**:530 (Oct.) 1927.

Syphilitic Appendicitis. J. Mesa y Gutiérrez, Gac. méd. de México **58**:467 (Aug.) 1927.

Syphilitic Meningitis in Infants and Young Children. J. W. Amesse and W. W. Barber, Am. J. Syph. **11**:544 (Oct.) 1927.
Syphilitic Periostitis. J. May and J. A. Pereyra, Rev. méd. d. Uruguay **30**:476 (Sept.) 1927.
Syphilitic Reinfection and Chancre of Tonsil. S. Grezzi and V. C. Paullier, An. de Fac. de med., Montevideo **12**:442 (July-Aug.) 1927.

Testing Hepatic Function in Syphilis. H. Biberstein and W. Scholz-Sadebeck, Arch. f. Dermat. u. Syph. **153**:755 (Oct. 23) 1927.
Therapeutic Malaria in General Paresis. J. F. McFadden, J. Missouri M. A. **24**:525 (Dec.) 1927.
Treatment of Cerebrospinal Syphilis: Typhoid Therapy. H. A. Cotton and J. M. Mras, J. M. Soc. New Jersey **24**:701 (Dec.) 1927.
Treatment of Early Syphilis. H. B. Decker, J. M. Soc. New Jersey **24**:681 (Dec.) 1927.
Treatment of Late Syphilis, Exclusive of Neurosyphilis. E. D. Newman, J. M. Soc. New Jersey **24**:683 (Dec.) 1927.
Treatment of Neurosyphilis. J. L. McCartney, Am. J. Syph. **11**:550 (Oct.) 1927.
Treatment of Syphilis. A. L. Anderson, Am. J. Syph. **11**:588 (Oct.) 1927.
Treatment of Syphilis. A. Ravogli, Am. J. Syph. **11**:576 (Oct.) 1927.

Value of Wassermann Reaction in Milk. H. Franken and H. G. Rottmann, Monatschr. f. Geburtsh. u. Gynäk. **77**:163 (Oct.) 1927.

Wassermann Reaction in Cerebrospinal Fluids Containing Blood. A. G. Foord and M. Bauckus, J. Lab. & Clin. Med. **13**:270 (Dec.) 1927.

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